“ASSOCIATION BETWEEN PLATELET INDICES AND ACUTE CORONARY SYNDROME IN A TERTIARY CARE CENTRE - A COMPARATIVE STUDY”

BY

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DEPARTMENT OF GENERAL MEDICINE

SREE MOOKAMBIKA INSTITUTE OF MEDIL SCIENCES

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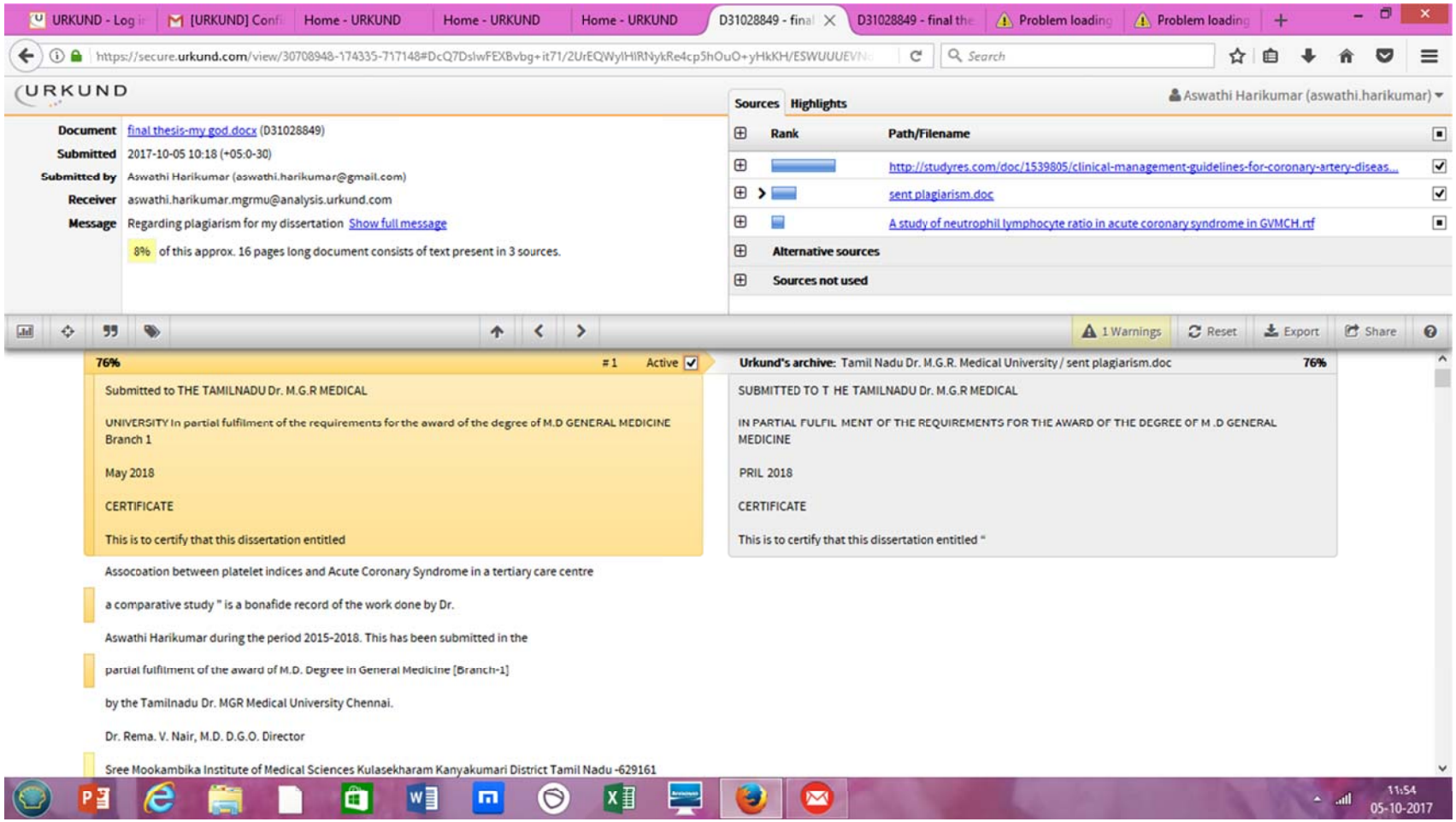
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ABSTRACT

BACKGROUND AND OBJECTIVES

A positive association between platelet indices and the development of acute coronary syndromes has been reported. The aims of the study were to compare the platelet indices in patients with ACS and those with non cardiac chest pain and to study other risk factors which took part in the development of ACS.

METHODS

Ethical committee clearance was obtained .After taking consent eighty five patients with ACS were taken and 85 patients with non cardiac chest pain were selected for the study. All subjects were in the group of 35-70 years. They were further divided into groups based on age, gender , BMI , history of diabetes, total cholesterol, family history, history of hypertension .These groups were studied for influences on ACS. The association of platelet indices such as mean platelet volume (MPV), plateletcrit (PCT) ,platelet distribution width(PDW) with ACS were studied. The data was analysed by SPSS version 20.0

RESULTS

The mean MPV of study participants with ACS were 12.468. The mean MPV of study non ACS patients were 10.636 .The mean PDW of study participants with ACS were 19.134. The mean PDW of study participants

without ACS were 13.611. The mean PCT of study participants were in ACS patients was 3.1. The mean PCT of study participants who had no acute coronary event were 2.19 .

CONCLUSIONS

Platelet indices had significant variation in patients with ACS. Patients of male gender were also presented frequently to the casualty with chest pain and were diagnosed to have ACS than females. Diabetes also significantly contributed to development of ACS. Higher total cholesterol was aculprit in the development of acute cardiac events. A patients BMI was also significant risk factor. Therefore platelet indices can be used as a economic marker of an acute coronary event .

Keywords : platelet indices, ACS

LIST OF CONTENTS

INTRODUCTION

Acute coronary syndrome (ACS) is a spectrum of conditions due to decreased blood flow in the coronary arteries such that part of the cardiac muscle is not able to function properly or dies and that is a result of platelet rich coronary thrombus formation.[1]

Plateletsfor long time have been implicated in the pathogenesis of cardiovascular diseases including atherosclerosis and its complications such as acute myocardial infarction, unstable angina and sudden cardiac death. Platelet hyperactivity and local platelet activation have been found to play a role in acute coronary events.[2]

Activated platelets are larger in size, and they can be measured by mean platelet volume (MPV)[1] .When platelets are larger, they become metabolically and enzymatically active. Platelet indices corresponds to functional status of platelets and is an emerging risk factor for atherothrombosis.[2]

Increased platelet activation may also represent the net patho - physiological effects of a number of cardiovascular risk factors, such as smoking and dyslipidaemia, thus representing a broad marker of CVD risk. Platelet activation leads to a more spherical shape with increased platelet swelling and thereby leading to an increase in platelet mass and volume.[3]

Free arachidonic acid is also formed due to platelet activation, which may be converted into prostaglandins, also known as thromboxane A2. It

isone of the most potent vasoconstrictor and platelet-aggregating substances, or into leukotrienes, which amplifies the acute inflammatory response.

Platelet function and size correlate because larger platelets, produced from activated megakaryocyte in the bone marrow, are likely to be more reactive than normal platelets because large platelets contain more of secretary granules and mitochondria and are known to be more active thanthe smaller platelets (normal).[3]

Large platelets are metabolically and enzymatically more active than smallerones and secrete and express more mediators such as adhesive proteins (fibrinogen, thrombospondin, and fibronectin), growth factors (plateletderived growth factor, transforming growth factor, and basic FGF), and chemotactic and mitogenic factors (platelet factor 4, coagulation factors [factor V and factor XI], and cytokinelike factors [interleukin1 and CD40ligand].[5]

Larger platelets as measured by their volumes (MPV) may be useful markers in patients with ACS.Higher MPV may become useful marker for early detection of ACS along with other biomarkers.

Patients with increased MPV could be easily identified during routine haematological analysis. It could play an important role in early detection of acute coronary syndrome (ACS) and beneficial for preventive treatment. It could be used as a screening test to differentiate the origin of chest pain along with other cardiac biomarkers.

A few reports published have revealed a larger MPV in Indian patients with ACS compared with healthy controls or patients with stable coronary artery disease.[4]

Unlike all other markers of platelet activation and reactivity, it is automatically calculated by most equipment for performing blood cell count.[5] Thus, to determine the platelet sizethrough MPV is a simple, extremely inexpensive, and readily available measure in hospital and outpatient settings.[5]

The commonest finding of ACS is ST elevation MI. Analysis of PVI indicated MPV & PDW as an important risk factor for developing a myocardial infarction. This was along with the elevated cardiac enzymes levels.[2]

MPV had higher sensitivity and specificity when compared to platelet count. MPV maybe used as predictor for early detection of ACS and risk stratification when other cardiac biomarkers are negative.[1]

Platelets with higher PCT and PDW were at higher risk of ACS. These patients can easily be identified during routine hematological examination and the patients could possibly benefit from preventive treatment.[1]

AIMS AND OBJECTIVES

- To compare the platelet indices in patients with ACS and those with non cardiac chest pain.
- To correlate the platelet indices and patients diagnosed with Acute Coronary Syndromes.
- To study factors associated with variation of platelet indices in ACS and non ACS patients.

SCIENTIFIC JUSTIFICATION OF THE STUDY:

The WHO has given attention to the fact that coronary artery disease is a modern epidemic more in geriatric population, that is, people above 60 years of age. An increase in coronary artery disease has been bought into the light and now it is the most common cause of death.

Previous data suggests that only 1/3rd of chest pain cases require critical care and hospitalization but in the absence of segregation of these cases in the beginning, physicians over admit such patients and it burns out the precious resources in the public setup. Further it may hamper the quality of care for those who actually require it.[9]

Platelet indices is a simple and economic laboratory measurement (less costly and can be done when a complete blood count is already requested), we suggest that it might be useful as an assisting rule-out test in conjunction with other conventional biochemical cardiac markers in the early prediction of the risk of ACS in patients admitted to the emergency department.

Hence, in this protocol we are doing a hospital based study to find out the changes that occur in platelet indices to provide early diagnosis of an acute coronary event. Moreover a study in this topic has not yet been done in the Kanyakumari district of Tamilnadu, India**.**

REVIEW OF LITERATURE

WORLDWIDE BURDEN OF ACUTE CORONARY SYNDROME

Ischemic heart disease (IHD) is the single major cause of mortality and loss of disability adjusted life years (DALYs) in the whole world, accounting for roughly seven million deaths and129 million DALYs annually.When high-income countries (HICs) continue to deal with significant IHD mortality, almost two-thirds of all IHD DALYs and over half of deaths occur in LMICs. Many of these countries have undergone exponential economic growth and lifestyle changes over the past several years that have increased theburden of IHD risk factors and rates of mortality.[47]

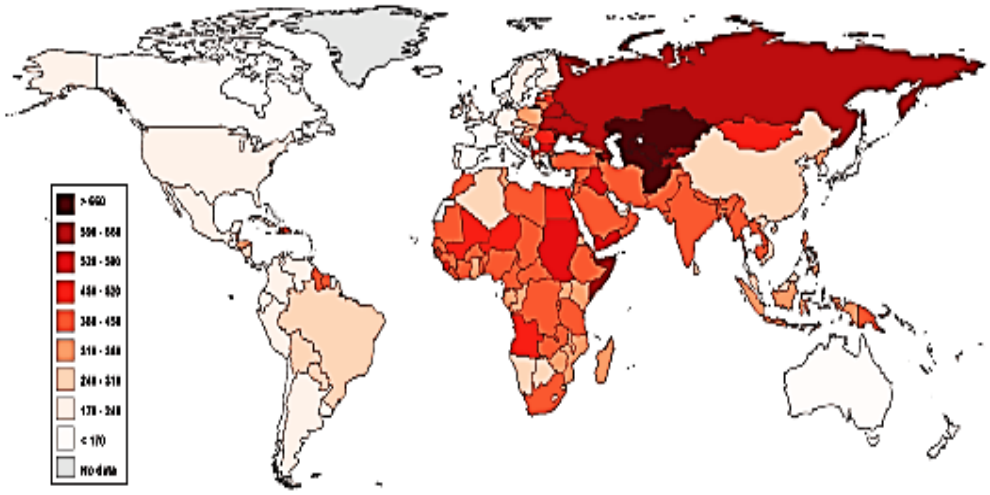


FIGURE 2.2 Age-standardized deaths due to cardiovascular disease (rate per 100,000), 2004.
NOTE: Rates are age-standardized to WHO's world standard population.
SOURCES: WHO, 2009e; map created with StatPlanet (van Cappelle, 2009).

FIG.1: Worldwide Burden of Acute Coronary Syndrome[47]

Overtwelve million people are diagnosed as ischemic heart disease andmore than one million have acute coronary events each year, resultingin about 466,000 deaths annually attributed to coronary artery disease. In Brazil, according to statistics, in 2008, 195,450 individuals wereadmitted with a diagnosis of Acute Myocardial Infarction (AMI)and other ischemic heart disease and 94, 912 deaths recorded.[48]

BURDEN OF CARDIOVASCULAR DISEASES IN INDIA

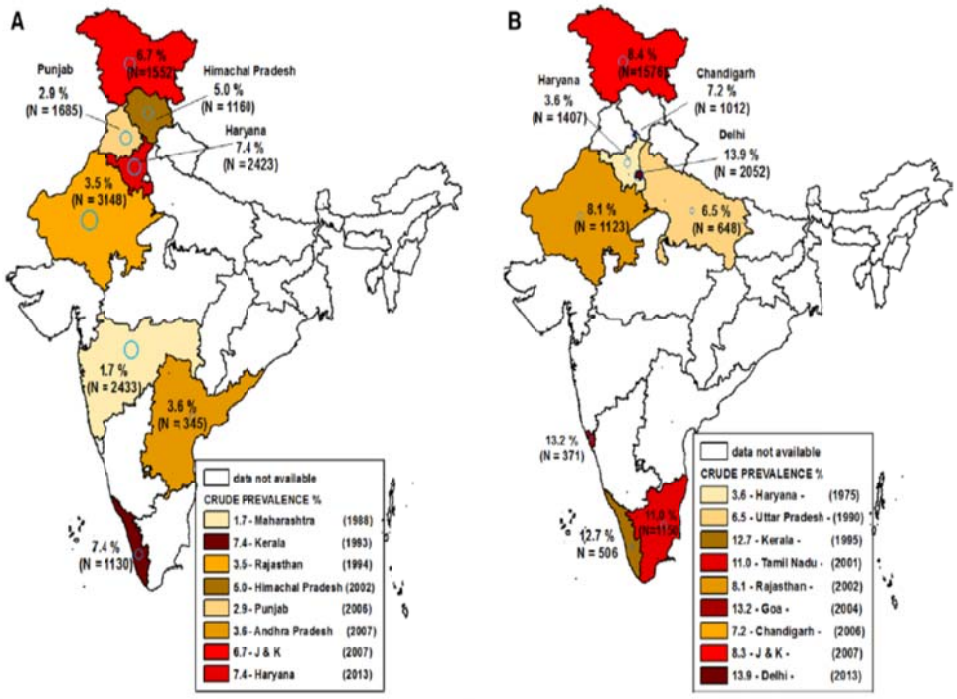


Figure 3. A, Ischemic heart disease prevalence rate in rural India. The numbers in the map are the prevalence; the sample sizes are in parentheses. The years of the source data are listed in the figure key in parentheses. Data from a new study in rural Haryana (2013) are included (D. Prabhakaran, unpublished data, 2013). B, Ischemic heart disease prevalence rate in urban India. The numbers in the map are the prevalence, with sample sizes in parentheses. The years of the source data are listed in the figure key in parentheses.

Fig 2 :Burden of cardiovascular diseases in India [21]

According to the Global Burden of Disease study age-standardized estimates (2010), almosta quarter (24.8%) of the mortality in India can be attributed to CVD. The age standardized CVD death rate of 272 per 100 000 population in India is more than the global average of 235 per 100 000 population.

Eventhough CVD risk factors are widely prevalent in India, there are significant variations between and within different regions. Diabetes mellitus is found to be more prevalent in the southern states of India, whereas hypertension seems to be higher in the northeastern states. This heterogeneity can be related to diversity in culture (leading to differences in dietary practices, tobacco use, and physical activity) and variations in economic development between and within different regions of India. Spectrum of ACS in North Eastern India and has noticed few key differences from national registry, which has greater percentage of STEMI patients, a greater delay in seeking critical care, greater 30-day mortality, and lesser percentage of patients receiving reperfusion therapy.[16]

Facing the epidemic requires the development of plans such as the formulation and effective implementation of evidence based policy, reinforcement of the medical systems, and more stress laid on prevention, early detection, and treatment with the help of both conventional and innovative techniques. Many ongoing community-based studies are verifying

these strategies and within different states in India, it is important to understand the social determinants.[21]

Patients with ischemic heart disease are divided into two large groups: patientswith chronic coronary artery disease (CAD) who most commonly present with stable angina and patients with acute coronary syndromes (ACSs) . These consists of patients with acute myocardial infarction with ST-segment elevation (STEMI) on their presenting electrocardiogram and those with non ST segment elevation acute coronary syndrome (NSTE-ACS).

The second group include patients with non-ST -segment elevation myocardial infarction (NSTEMI), whoby definitionhave finding of myocyte necrosis, and those with unstable angina (UA), who do not. The incidence relatively of NSTEMI compared to STEMI appears to be on the increase.[23]

CLINICAL PRESENTATION

Diagnosis

The diagnosis of NSTE-ACS depends largely on the clinical presentation. Usually, chest discomfort is severe and has at least one of three clinical features:

1. It occurs at rest (or with minimal exertion lasting for more than 10 minutes)
2. It is of recent onset (i.e. within the prior 2weeks); and/or
3. It occurs with a crescendo pattern (i.e. more severe, prolonged, or frequent than previous episodes) .

The diagnosis of ACS is confirmed if a patient with these clinical features develops evidence of myocardial necrosis, which is reflected as abnormally elevated levels of biomarkers of cardiac necrosis.[23]

THE PATHOPHYSIOLOGY OF ACUTE CORONARY SYNDROMES

The importance of thrombosis as the trigger for acute myocardial ischaemia is well known, it is of great use to know something about the structure of plaques before thrombotic events occur and why there is a sudden change from a stable state (where there is no thrombus) to an unstable state (thrombus).[24]

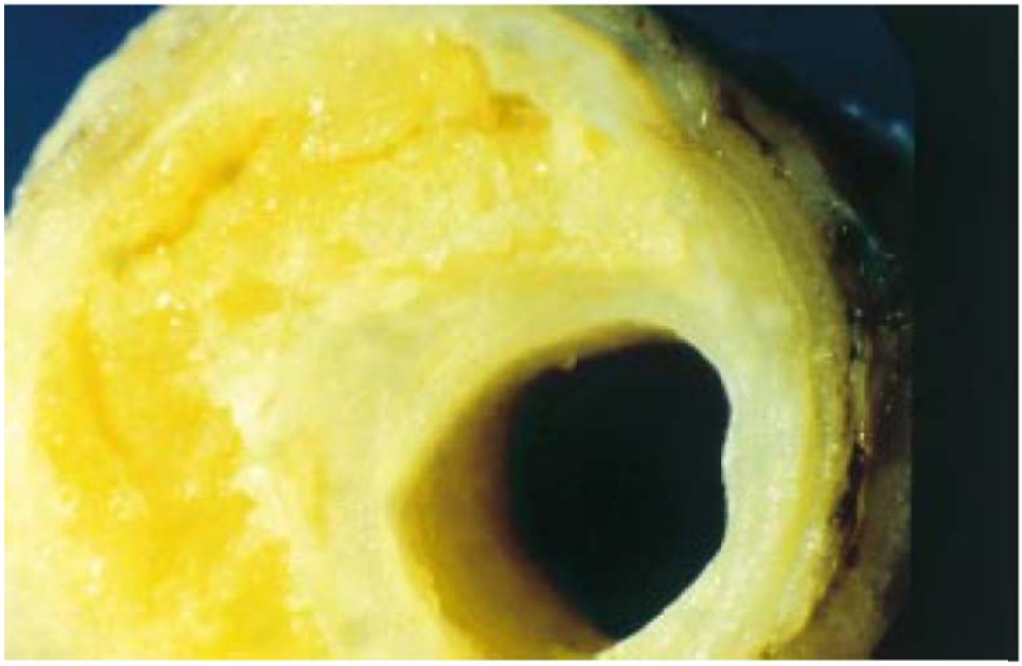


Figure 1: The established stable plaque. In this cross section of a human coronary artery there is an established fibrolipid plaque with a core of lipid. The lipid core is separated from the lumen by the plaque cap. The plaque only occupies part of the circumference of the artery, leaving a segment of normal arterial wall.

Fig3: The Chronic Stable Plaque[24]

Atherothrombosis

Thrombus formation which is localized and vasoconstriction are homeostatic responses to microvascular damage. Atherothrombosis is defined as atherosclerotic plaque disruption with a superimposed thrombus is said to be the leading cause of mortality in the Western world. It is what clinically manifests as coronary artery disease, cerebrovascular accidents , transient ischemic attacks (TIA) and peripheral artery disease.[24]

Atherosclerosis

It is described as a "response to injury" which was first suggested by Russell Ross in 1973. There are four steps in his model:

1) Endothelial damage,
2) Migration of LDL particles through the endothelial layer into the intima where they are modified,
3) Inflammation mediated responses,
4) Formation of a fibrous cap.

Theendothelium is prone for damage by various factors such as hypertension, type 2 diabetes mellitus, tobacco, infections, or even oxidative and shear stress.[24]

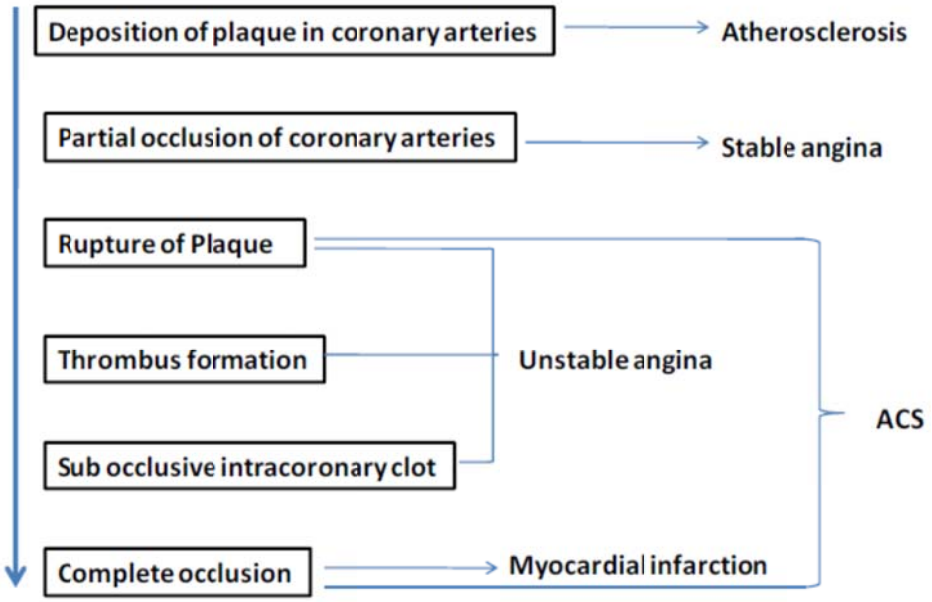


Fig3:The pathogenic spectrum of CAD[24]

History and Physical Examination[23]

The chest discomfort, is often severe enough to be described as frank pain, is usually located in the substernal area or sometimes in the epigastric area, and radiates to the left arm, left shoulderor neck.

Anginal "equivalents" such as breathlessness, epigastric discomfort, nausea, or tiredness may occur instead of chest pain and appear to be more frequently seen in women the elderly, and in those with diabetes mellitus. The physical examination resembles patients with stable angina and may be unremarkable.

If the patient has a large patch of myocardial ischemia or a large NSTEMI, the physical findings will be diaphoresis; pale, cool skin; sinus tachycardia; a third and/or fourth heart sound; basilar rales; and occassionally, hypotension.[23]

ELECTROCARDIOGRAM IN CAD

- **A 12 lead resting ECG** (± RV3, RV4 for right ventricular MI) should be taken immediately in patients with ongoing chest pain as early as possible within 10 minutesof presentation.
- A **normal ECG which may not be consistent even in the** presence of severe CAD, and ECG should be taken or repeated ifstrong suspicion in every 4-6 hours or earlier.

ECG abnormality includes:

- ❖ Resting **ST segment changes** (depression ≥ 0.5 mm horizontal or downsloping in NSTEMI, convex elevation > 1mm in ≥2 consecutive leads in STEMI, pseudonormalization of ST segment or dynamic changes).
- ❖ New pathological **Q-waves** (>0.4 seconds) is usually diagnostic of MI, but may occurwith prolonged ischemia.
- ❖ **T wave**-inversion (≥ 2 mm symmetrical) or a peaked upright T waves may be the firstECG changes of Myocardial Ischemia.
- ❖ New onset **LBBB**

- **Right ventricular myocardial infarction** is diagnosed with ST segment elevation in lead V4R, ST elevation in V1 along with ST elevation in inferior leads.
- **Non-specific ST and T changes:** ST depression <0.5 mm, T wave inversion <2mm,isoelectric T wave or asymmetric T inversion is less likely of myocardial ischemia.
- The **range of normal ST-segment** deviation differs between men and women. STelevation(concave upwards) in the V2 or V3 leads of 2·0 mV or less in men and 1·5 mVor less in women, or 1·0 mV or less in other leads, is normal
- ECG **changes that may mimic MI** results from pre-excitation, pericarditis, myocarditis,cardiomyopathy, COPD, pulmonary embolism, cholecystitis, and hyperkalemia; which the physicians should be aware of .[26]

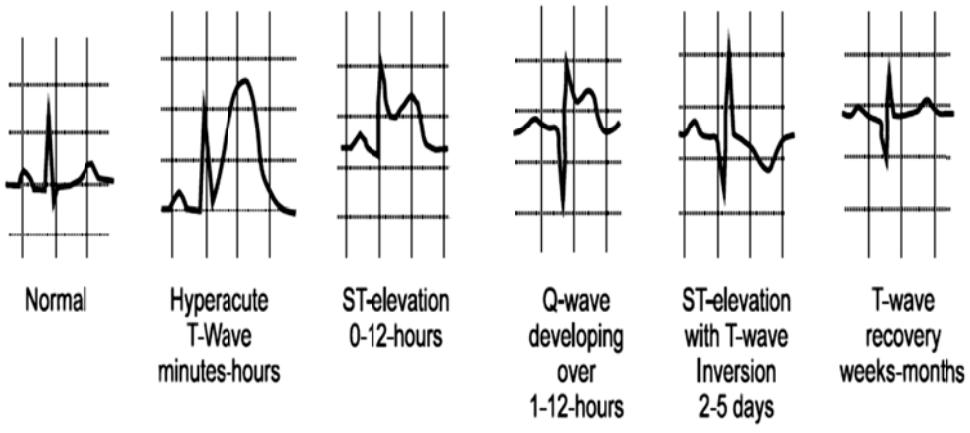


Fig 4:ECG variations during myocardial infarctions[26]

LABORATORY STUDIES[26]

- **Blood samples** should be sent for cardiac enzymes (biomarkers Troponin I or T and CKMB) for confirmation of ACS; complete blood haemogram, blood urea, creatinine, electrolytes, FBS –formonitoring and Fasting lipid profile- for secondary prevention. Cardiac specific troponinis the preferred biomarker for diagnosis of STEMI. The advantage of Troponin I is that it does not alter with renal failure.A portable **chest radiograph** is useful to exclude other non cardiac causes of acute chest pain but itshould not delay the treatment.
- **Imaging:2D echocardiography**: Abnormalities of wall motion are almost alwayspresent in STEMI. Estimation of left ventricular (LV) function is usefulin the long run . It identifies the presence of right ventricular (RV)infarction, ventricular aneurysm, pericardial effusion, and LV appendage thrombus.
- **Doppler echocardiography**: it is useful in detection and quantification of aventricular septal defect and mitral regurgitation.[26]

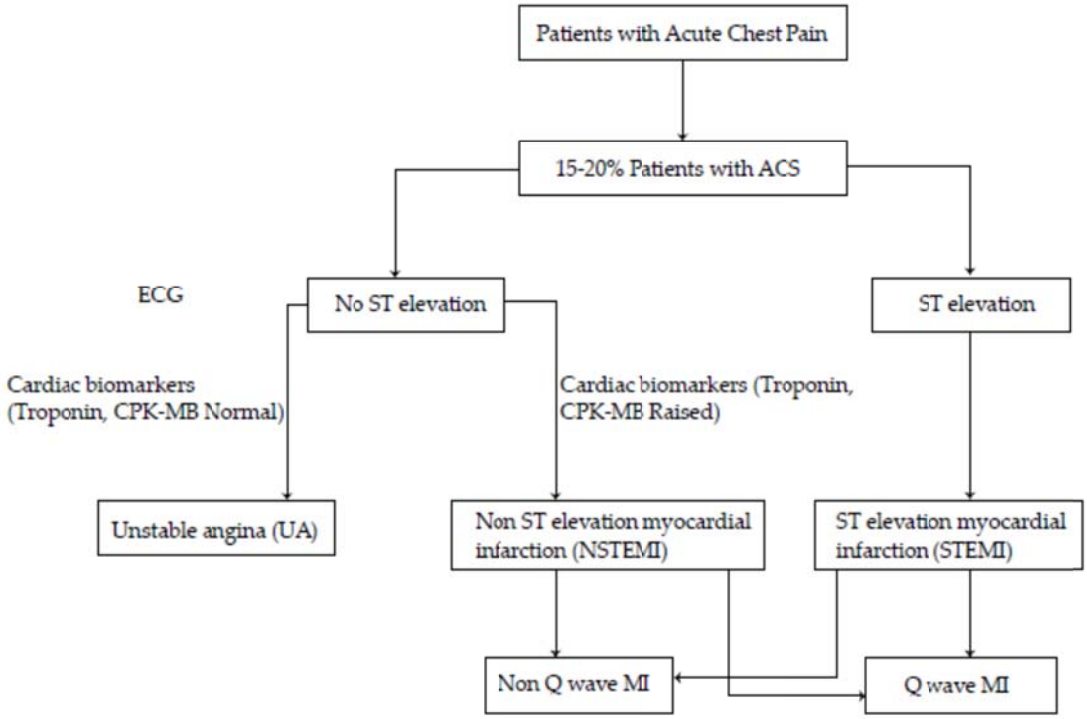


Fig 5:Approach to patient with acute chest pain[27]

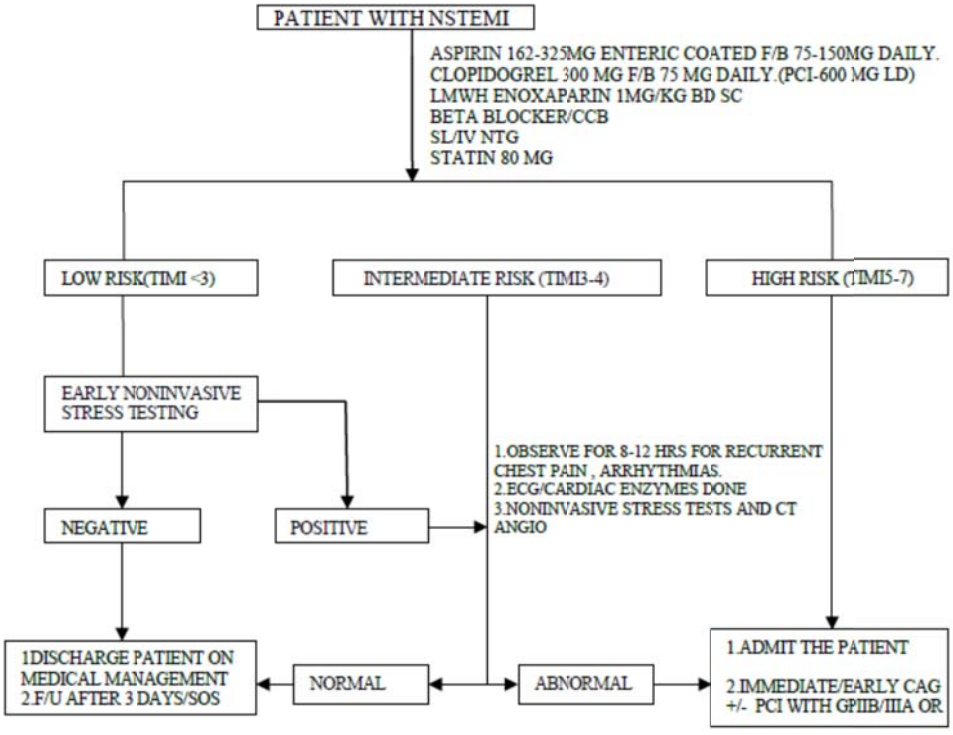


Fig6: Approach to patient with NSTEMI[27]

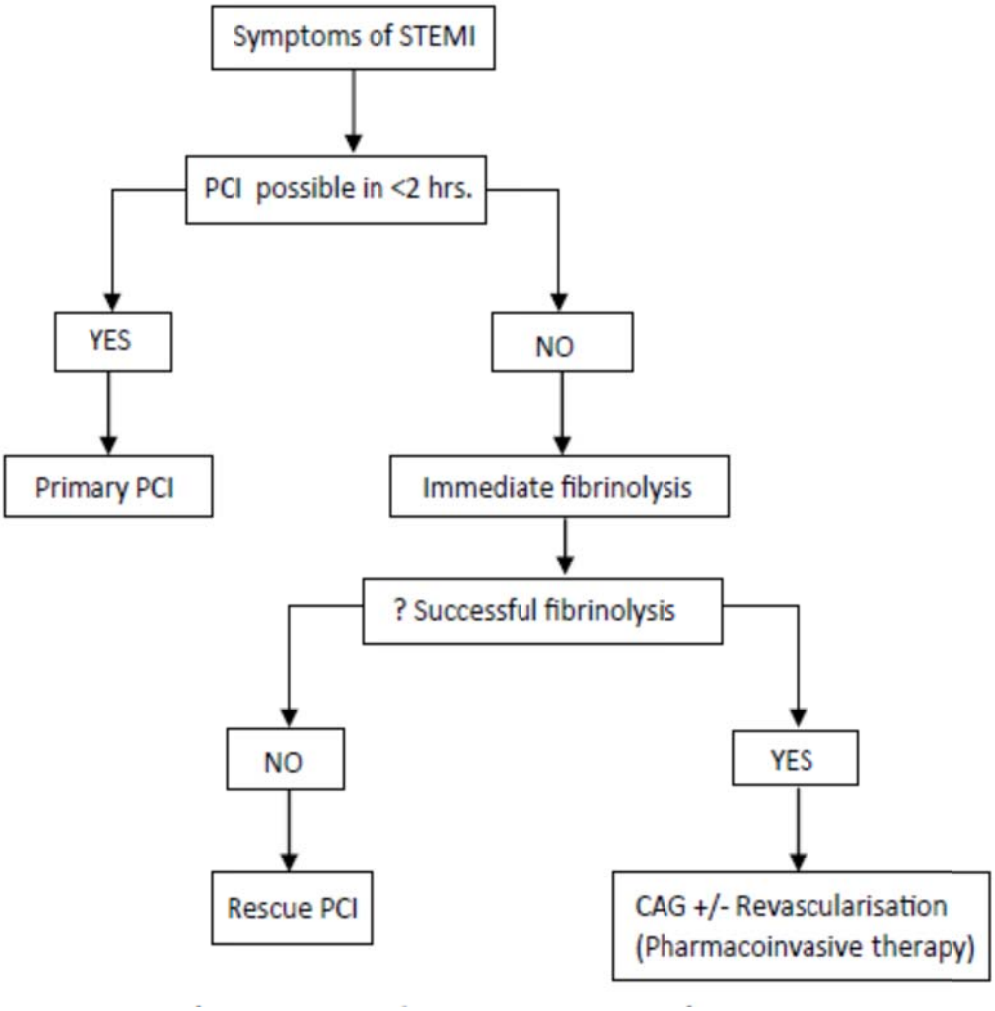


Fig7: Approach to patient with STEMI[27]

Management of patients diagnosed with NSTEMI

Those patients with probability of NSTE-ACS and who are stable should be admitted on an inpatient basis for bedrest with continuous monitoring of rhythmand careful observation for any recurrence of ischaemia . High risk patients, especially those with continuing discomfort and/or haemodynamic instability, should beimmediately shifted to a coronary care unit (CCU)and observed for at least 24-48 hours.Fibrinolytic (thrombolytic) therapy which uses streptokinase, urokinase, tenecteplase orany other agent should not be instigated inpatients with UA and NSTEMI. Theseagents may definitely prove harmful. GlycoproteinIIb/IIIa agents like abciximab, tirofibanandeptifibatide are seen to be useful inpatients undergoing percutaneous coronary interventions (PCI).

1)Anti- ischemic and analgesic medications

Oxygen is very useful for initial stabilizationspecifically in those with hypoxemia.

Topical, oral or intravenous nitrates are very useful for pain relief. Intravenous nitroglycerin (NTG) is helpful in those who are resistant or unresponsive to sublingualNTG, in those with hypertension and heart failure. This drug should be used cautiously if systolic blood pressure is below 100 mm of Hg.

The nonsteroidal anti-inflammatory drugs (NSAIDs) andCOX-2 inhibitors is not recommended for pain relief. There is increased risk of cardiovascular events. The use of morphine also not specified in UA/NSTEMI.

Beta blockers are found to be useful for pain relief. The administration of intravenous beta blockers should be withheld particularly in unstable patients. Calcium channel blockers are of use in vasospastic angina and in patients who have contraindications to betablockade. Some of the other antianginal drugs like ivabradine, trimetazidine, ranolazine and nicorandil are found to Have very limited role.

2)Antiplatelet agents used in NSTEMI

Admintration of Aspirin to all patients unless contraindicated and as mentioned earlier, first dose of chewed non-enteric aspirin varying from 162 to 325 mg is given. Subsequent dose of aspirin can be 75 to 100mg daily which is on a long term basis. The chances of gastro intestinal bleeding appears to increase with higher doses.

Clopidogrel is given in all the patients with animmediate dose of 300 mg followed by 75 mg on a daily basis. In patients who are being planned for a PCI, a loading dose of 600 mg is advised to achieve more rapid inhibition of platelet function. Clopidogrel should be maintained for at least 12 months unless there is an increased risk of bleeding.

3) Current recommendations for Anticoagulant therapy

Anticoagulation therapyis strictly recommended for all patients in additional to antiplatelet agents. Many number of agentsare available which include unfractionated heparin (UFH),low molecular weight heparin (LMWH), fondaparinux andbivalirudin. The choice of drug mainlydepends on therisk of ischemic and bleeding episodes and the choice of the initialmanagement strategy (e.g. urgently invasive, early invasive or even when conservative).

Enoxaparin (1mg/kg bw twice daily) is the preferredanticoagulant and is a good option in patients who are treatedconservatively or even by invasive strategy. Enoxaparin is usually stopped within 24 h after an invasive strategy and it should be administered up to hospital discharge (usually 3 to 5 days)during conservative strategy.

Fondaparinux is used based on favourable efficacy/ safety profile and the recommended daily dosage of 2.5 mg . This agent has the least bleeding complications. An additional UFH in standard dose of 50-100 U/kg bolus ismandatory during PCI due to slightly high incidence of catheterthrombosis.

Statins are given for all NSTE ACS patients, irrespective of cholesterol levels, and is initiated early upon admission,with the main aim of achieving LDL C levels <70 mg/dL. Atorvastatin is usual agent which is preffered, at a dose of 80mg per day. ACE inhibitors are prescribed in patients with reduced LV systolicfunction. Whereas ARB's areonly indicated in those patients who are intolerant to ACE in hibitiors.

4)Coronary intervention

Revascularization for NSTE ACS is done to give relief from angina, ongoing myocardial ischemia and to prevent the progression to MI or death. The decision for revascularization as thepreferred approach, PCI or CABGS totally depends on the extent andseverity of the lesions, the patient's general condition and co-morbidities .

Approach in the long run

Patients diagnosed with NSTE ACS after the initial phase usually carry a highrisk of recurrence of ischemic events. Therefore, anactive secondaryprevention is an essential componentof long term management.

Life style modification, weight loss, strict blood pressure control and monitoring, control and management of diabetes, lipid profile intervention, antiplatelet therapy ,beta blockers, ACE inhibitors (or ARB) remain to be watched out for.

Management of patients diagnosed with STEMI

The initial treatment that should be given is 325 mg of(preferably) non enteric-coated aspirin which can be chewed. Irrespectively all patients should receive aspirin. Clopidogrel is administered as a loading dose of 300 to 600 mg to all the patients. Patients who are going to undergo primary PCI should receive a 600 mg loading dose.

All patients should be given medications to relieve pain. It may include opioid analgesics (morphine sulfate intravenously). Sublingual or intravenous nitrates can be administered if systolic blood pressure is ≥120 mm Hg.

But if systolic BP is ≥100 mm Hg but less than 120 mm Hg,then nitrates should be administered cautiously. Non-steroidal anti-inflammatory drugs. (NSAIDs, other than aspirin) is not be given for analgesia.

Reperfusion therapy is said to be the cornerstone of STEMI management and should be initiated in all the patients presenting within 12hours of onset of symptoms. The most effective reperfusion therapy available is timely primary PCI, but it may not be as effective in the Indian context when compared to the western population , given to the relative deficiency of PCI-capable centers. Moreover, since most of these centers for PCI are located in the urban areas, the distances involved in transporting patients from rural are as to urban becomes time consuming. Fibrinolytictherapy therefore remains the most effective practicable reperfusion treatment strategy for India.

Fibrinolytic therapy in STEMI patients

As a norm , streptokinase is the most frequently used fibrinolytic agent in India. Recently, there has been some favorable evidence for the use of Tenecteplase in Indian settings. Tenecteplase has been found to be fibrinspecific,can be given as a bolus dose, and has a lower incidenceof allergic

reactions. Tenecteplaseis usually administered at a dose of 0.5 mg/kg body weight.

Immediate Transportation of Patients to Centers equipped with CCUs and/or PCI

The delay to access the hospital can be reduced by institutionof systems to be initiated as pre-hospital protocol and fibrinolysis.Pre-hospital fibrinolytic therapy has clearly proved to improveoutcomes as compared to primary PCI.But recently studies in Europe and North America have shown that transport of patients to PCI-capable centers may be a betterstrategy than immediate fibrinolytic therapy. But such may not be suitable for most parts of India becauseof the long distances that are involved and the difficulty oftransport. But still , it may be possible for small urban and rural to develop systems for the provision ofefficient services for transporting such patients to designated PCI capable centers.

After the administration of fibrinolytic therapy some situations may necessitate transfer of such patients to such centers those indications are:

1. Those patients who are in cardiogenic shock or those who are at high risk of developing the same.
2. Those patients with failed fibrinolytic therapy
3. High-risk patients.

Antiplatelet therapy in STEMI patients

Aspirin and clopidogrel should be given per oral as initially discussed. That is maintenance dose aspirin (75-100 mg) and clopidogrel (75 mg) should be given.

As per the latest ACC/AHA guidelines, GlycoproteinIIb/IIIa antagonists can be selectively used in patientsundergoing primary PCI I when in the setting of dual antiplatelet therapy with UFH is used as the anticoagulant inthe catheterization laboratory, during the procedurewhere large thrombus burden is present or patient has received an inadequate thienopyridine loading.

There is no role of administration of these agents to bridge the time delay before primary PCI(facilitated PCI). Abciximab, eptifibatide and tirofiban appear to be as effective and can be used depending upon the treating physician's preferences and availability.

Antithrombotic Therapy

After the treatment with both fibrin-specific and non fibrin specific fibrinolytic agents, there is strong indication for the usage of antithrombotic agents for reducing reinfarction or recurrent schemia. Recent studies havesuggested that low molecular weight heparins (LMWH) can be better than unfractionated heparin(UFH) and for this purpose,the LMWHs

Enoxaparin or reviparin

Can be administered even for up to 8 days post-MI. Fondaparinux has been shown to decrease the occurrence of mortality or reinfarction while side to side reducing the risk of major bleeding, and may therefore be considered in patients who are undergoing treatment with streptokinase.There seems to be no role forbivalirudin among patients who are on fibrinolytic therapy. Patients are to undergo primary PCI should receive peri procedural UFH26 or bivalirudin. Fondaparinux (without added UFH) is found to increase the risk of catheter thrombosis.

Beta Adrenergic Antagonists

Oral beta-blockers is usually administered by the first 24 hoursto patients who are not in heart failure, or a low output state, or not at an increased risk of having cardiogenic shock, or those who donot have other contraindications to beta-blocker therapy.In case ACEinhibitors and ARBs', care should be taken to avoid hypotension.

ACE inhibitors are found to improve survival in those patients who have reduced left ventricular ejection fraction (LVEF ≤40%) and in those who are in heart failure following acute coronary event . Benefits areproportionately lower among low risk patients. ACE inhibitors are to be started in the first 24 hours after STEMI unless contraindicated . ARBs can be used in patients who do not tolerate ACE inhibitors.

Use of intravenous or oral nitratesis shown not to improveoutcomes in patients with STEMI. Nitrates can be used for pain relief. There has been no role for the routine use of calcium antagonists,intravenous magnesium, and antiarrhythmic drugs or glucoseinsulin-potassium infusions, and these therapies may be associated with adverseoutcomes in some cases. High doses of statins should be started as early as allowed during hospital stay as part of se prevention measures. The dose of statin used in Indian patients is not studied , but lowering LDL levels to ≤80mg/dL may serve as a useful target.

Many studies have suggested that routine angiographyand PCI of the infarct related artery may decrease the chances of reocclusion or reinfarction. Some other recent data clearly suggests that Pharmaco-invasive therapy has an important place in the improvement of the prognosis of patientsafter thrombolysis. Unlike facilitated PCI after which patients are immediately taken up for PCI after thrombolysis.

It has been increasingly been seen that patients after a successfulthrombolysis are to be transferred to facilities with cardiac cath laboratory for coronary angiography and, if needed, a PCIwith stent deployment.

However, because of the intensive resources used up for thisstrategy and in the absence of an effect on survival in many studies most guidelines still uphold a more conservative dimension which consists of

revascularization guided by the results of riskstratificationby means of early exercise stress testing.

FUNCTIONS OF PLATELETS[30]

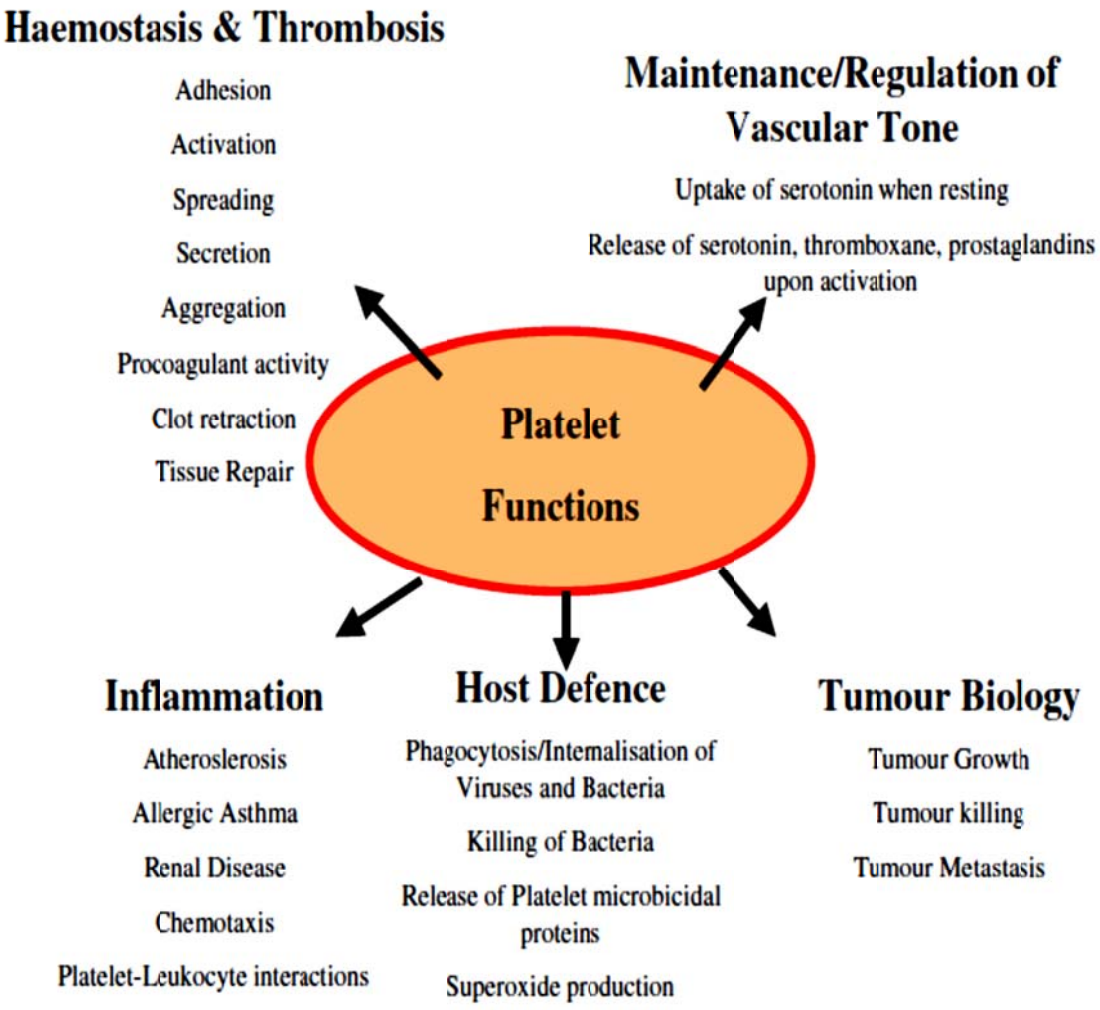
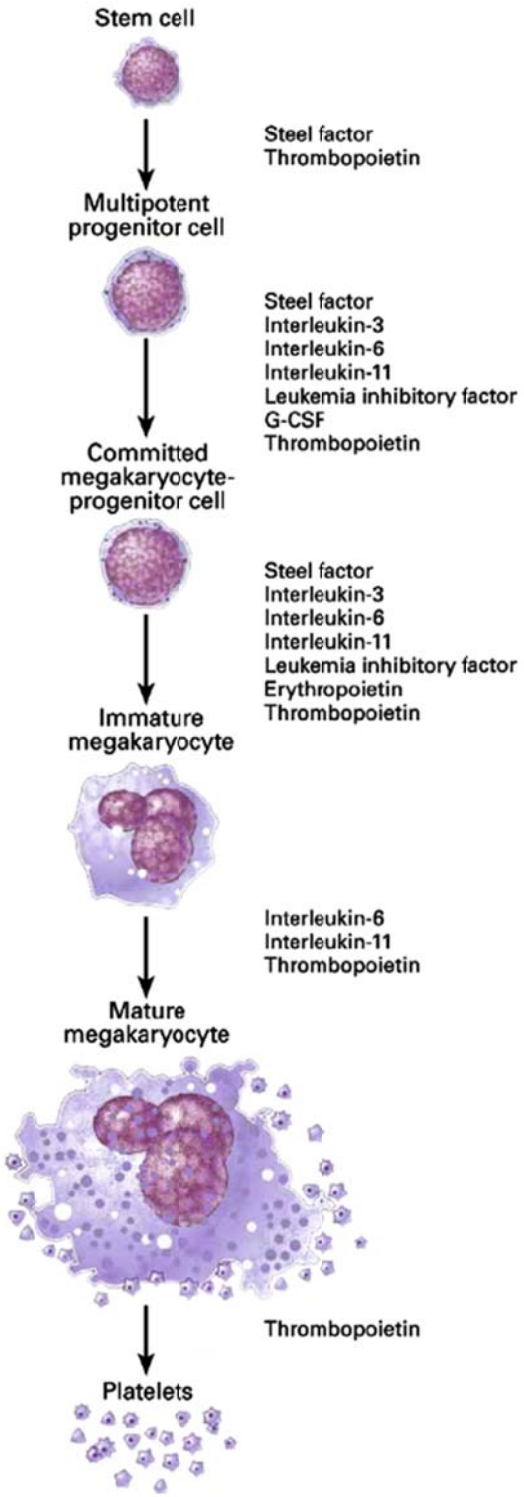


Fig 8: Platelet Functions[30]

DEVELOPMENT OF PLATELETS



PLATELET PHYSIOLOGY

Platelets take part in primary as well as secondary haemostasis. This process can be many stages, such as platelet adhesion, platelet aggregation and pro-coagulant activity .

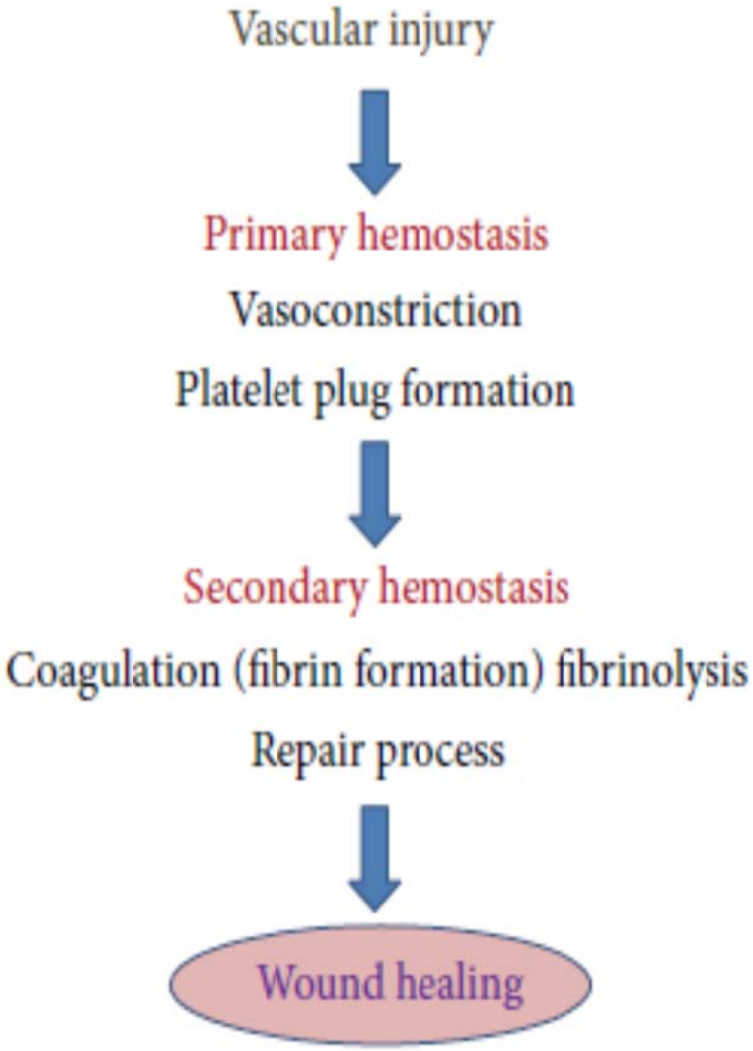


Fig 10:Pathway illustrating Haemostasis[35]

Platelet adhesion[35]

In response to endothelial damage the platelets, which usually circulate in an isolated fashion, instead adhere to the subendothelial matrix. This causes interaction between platelet membrane glycoproteins and adhesive protein from the endothelium, collagen and the Von Willebrand factor (VWF).

Under reduced flow conditions, this interaction is conducted by GPIa-IIa platelet glycoprotein; under turbulent flow conditions, the GPIb-IX-V complex participates.

GPVI (62 kDa) belongs to the class of immunoglobulin superfamily and, along with GPIa-IIa, acts as a collagen receptor. On the surface of the platelet, it forms a complex with the receptor Fcγ, activating the phosphorylation of a cytoplasmatic segment of the receptor and thereby causing platelet activation.

The GPIb -IX complex (CD42b, CD42a, CD42d) functions as a receptor for FVW, taking part in the platelet adhesion process. Resting platelets express ~25,000 copies of this glycoprotein complex .

Platelet aggregation.[35]

When the platelets have adhered, they assume a spherical form with extensions that exhibit the GPIIb-IIIa complex, forming dimers of the glycoprotein to attach the fibrinogen or FVW, according to the flow, and to release the content of their granules. This activates and adds more platelets

The GPIIb-IIIa complex (integrin αIIbs3, CD41-CD61) is a 228-kDa heterodimer whose structure consists of an extracellular domain as a transmembrane and a small cytoplasmatic domain. Every single platelet displays ~40,000-50,000 copies of this glycoprotein complex.

As well as binding fibrinogen and FVW, the GPIIb-IIIa complex it can also bind to fibronectin and vitronectin, thus taking part in the adhesion and aggregation of the platelet mechanism.

Platelet secretion[35]

There are two types of granules which are functionally the most important in platelets: α granules and dense granules. Alpha granules store large amounts of proteins, among them fibrinogen, FVW, platelet factor 4 (PF4), GPIIb-IIIa, FV, FVIII, FXI, platelet-derived growth factor (PDGF) and epidermal growth factor (EGF), which takes part in platelet aggregation. Whereas dense granules are rich in calcium, phosphorus, ADP and ATP; the release of dense granule content has a special place in the amplification of the platelet response.

Pro-coagulant activity[35]

Lipid deposition in the platelet membrane is of functional importance. Two enzymes, a translocase specific to aminophospholipids and a flopase, maintain the asymmetric state of phospholipids in the membrane.

During the activation of platelets, there will be a redistribution of anionic phospholipids, mainly phosphatidylserine (PS), which occurs from

inside to outside by the action of the enzyme scramblase , which is activated by the increase in cytosolic calcium of platelets and creates a surface with a anionic electric charge .

This favours the formation of coagulation complexes and, consequently, the formation of fibrin and the consolidation of the thrombus.

PLATELET DISORDERS

Disorder of platelet adhesion :

1)Ehlers-Danlos Syndrome

It is one of the inherited disorders of collagen biosynthesis, such as the Ehlers-Danlos syndrome which is characterized by extremely fragile skin and easy bruisability. Such patients may sustain severe and extensive ecchymoses even from minimal trauma. While looking into Ehlers-Danlos syndrome type IV, there is a pronounced chance of easy bruising which may lead to sudden death from spontaneous hemorrhage as a consequence of arterial rupture. Abnormal bleeding has been thought to be the as a result defective connective tissues. For example, Ehlers-Danlos syndrome type IV is characterized by a deficiency of type III collagen in the skin and vessel wall.

Poor connective tissue linkage has more chances for vessel wall rupture, very poor vessel wall retraction after disruption and seepage of the hematoma along very fragile tissue planes. Intrinsic platelet function is usually seen to be normal in this syndrome, but defective platelet adhesion due to the

disrupted defective vessel wall impairs platelet plug formation and leads to a bleeding disorder simulating qualitative platelet defects. The diagnosis is suspected on clinical examination along with normal findings on in vitro tests of hemostasis.

SCURVY

Scurvy, is an acquired platelet disorder which is now rarely seen, may usually be associated with a significant bleeding diasthesis, which is the result of a connective tissue disorder caused by vitamin C deficiency. The deficiency of vitamin C impairs the synthesis of hydroxyproline, an important building material of normal collagen.

Theresultant defective collagen weakens the connective tissue, producing bleeding manifestations such as gum bleeding, and subcutaneous and intramuscular hemorrhages. It is characteristic of perifollicular petechiae.

The bleeding time can be slightly increased and invitro platelet function is normal. Scurvy responds within few weeks following oraladministration of vitamin C.

AMYLOIDOSIS

It is a disorder in which purpura may be acquired from the diffuse vascular and mucosal infiltration which occurs in systemic amyloidosis. Periorbital purpura is typical.

The chance of hemorrhage is higher after minor surgical procedures such as skin, gum or liver biopsy. When amyloidosis occurs in combination with plasma cell myeloma, the hemostatic defects resulting from the latter condition may again further increase the risk of bleeding tendency.

DISORDERS OF PLATELET ADHESION

Bernard-Soulier Syndrome

This syndrome is a rare, familialbleeding disorder which is of moderate severity characterizedclinically by mainly bleeding from the nose, menorrhagia, and cutaneous and visceral haemorrhages. The platelet count can be variable, and on the blood film the platelets is seen to be enlargeddue to their flat disc shape.

The bleeding time is significantlyprolongedthatis, more than 20 minutes. Ristocetin-induced platelet aggregation is not seen and can not be corrected by the addition of exogenous, von Willebrand factor. Other factors of platelet aggregation is normal .

The defective hemostasis in this syndromeis secondarydue to an intrinsic defect of platelet adhesionto subendothelium. The membrane glycoprotein of platelets from these patients shows reduced number of membrane glycoproteins designated GPIb and GPIs (glycocalicin).

There supportive evidence for the hypothesis that the absenceof these membrane glycoproteins is responsiblefor the observed functional defect. It has

been studied that this glycoprotein I complexusually acts as the platelet receptor through which the von Willebrand factor is a mediator not only the platelet subendothelium interaction but also in the vitro ristocetin-induced platelet aggregation .

Von Willebrand Disease

It is a common heterogeneous group of congenital bleeding disorders, in which an increased bleeding time and defective hemostasis are the result offactor VIII/von Willebrand factor (FVIII/VWF).

The disease's classic form isinherited as an autosomal dominant trait and it is characterized by a mild to moderatebleeding tendency that frequently involves bleeding from the nose (epistaxis), severe gum bleeding, menorrhagia or postoperativehaemorrhage . Gastrointestinal, muscle andjoint bleeding are uncommon .The bleeding time is prolonged. Biochemically, it can be divided into two main variants and is defined on the basis oflaboratory findings. In type 1 there is a simultaneous reduction in factors such as Ag and Co. In type 2, a qualitative defect of Factor 8/VWF complex can be shown on radiocrossedimmunoelectrophoresis, which shows the absence of the larger molecules of the above said complex.

An uncommon but more severe form of von Willebrand disease is passed over as an autosomalrecessive trait and it is similar to hemophilia.

Muscle, gastrointestinal and haemarthrosis, as well as bleeding from the are the most commonclinical manifestations. The disease is inheritedfrom both

the parents, eventhough the heterozygoteparents are most of the time clinically normal or have onlya mild bleeding tendency with modest abnormalities of the same complex. The template bleeding time in diseased patients is greatly increased .

Qualitative and quantitative defects of the complex can be seen oncrossed immunoelectrophoresis. Studies haverevealed that the Factor 8:Ag level is significantly reduced and a small amount of antigenthat is also present is abnormal configuration .

Uremia

It causes an extrinsic platelet defect due to the progressive rapid accumulation of metabolicproducts in the blood. In previously untreated patients with uremia the template bleeding time is prolonged for more than 30 minutes and, as predicted , reduces to near normal in those taken up peritoneal dialysis. Hemodialysis seems to be less effectivein this regard.

STUDIES RELATED TO ACS AND PLATELET INDICES

Ridavanet al. did a study in 2010 in Turkey on mean platelet volume and its association with acute coronary syndrome. From a population of 214 patients where69 were with acute MI, 73 were with unstable angina pectoris, 72 patients with stable angina pectoris and control group of 45 patients who had atypical chest pain with no pathological signs in coronary angiography. They found out that mean platelet volume was increased in patients Acute Coronary Syndrome.[6]

Pervin et al .did a study in Bangladesh in 2011 on 79 patients diagnosed with ACS based on clinical history, ECG and increased troponin I with 63 subjects as control. They found out that Mean Platelet volume (MPV) had higher sensitivity and specificity in contrast to platelet count and can be used for early detection of Acute Coronary Syndrome. The sensitivity, specificity , accuracy, positive and negative predictive value of platelet counts and MPV were 83%, 28.1%, 42.3%, 37.6%, 64% and 90.6%, 49.4%,64.8% 51.6% ,89.8% respectively.[13]

Tomasz et al.did a prospective study in 2013 in Poland on 538 patients who underwent primary PCI in acute MI. Admission samples were measures for MPV,PDW and P-LCR and were followed for 26+/-11 months and found out that MPV,PDW and P-LCR measured on admission are strong independent prognostic factors in PCI treated acute MI.[49]

Jasmin et al. did a comparative study at SBKS Medical Institute & Research Centre,Vadadora in 2014 on 180 patients (60 patients with stable angina ,60 with ACS and 60 with non cardiac chest pain). Platelet count and volume indices were assayed .In patients with MI ,the mean values of MPV, PDW ,platelet count and PC were 11.02fL ,17.85% ,2.61 lac/ cumm and 0.34% respectively ,meanwhile normal healthy control the mean values of those indices were 7.98Fl, 10.70%, 2.66lac/ cumm and 0.24%respectively.[7]

Randheer et al. did a study in 2014 in SMS Medical College , Rajasthan on 215 eligible patients to investigate whether there is an association between MPV measurement and cardiac Troponin I (cTn I) in patients with suspected diagnosis of ACS. Mean platelet volume (MPV) was found to be higher among ACS patients as compared to non ACS, 11.44±1.23 vs 9.91±1.27 fl (p-value<0.001). The NPV of MPV in the diagnostic workup of chest pain suggestive of ACS within 6 hours of presentation were found to be 82.53% .[9]

Murazsemiz et al .did a study in Turkey in 2012 in 60 hospitalized schizophrenia patients taking atypical antipsychotics to find out what has influenced the Mean Platelet Volume levels in patients with schizophrenia because cardiovascular diseases are more frequently encountered in in these patients compared with general population. MPV levelswere significantly higher in patients who were on atypical antipsychotics drugs than in patients who were not using any drugs (9.2+/-0.8 vs8.6+/-0.8Fl ,P=0.016) & also higher than in control groups(9.2+/-0.8 vs 8.1+/-0.9Fl,P<0.001).[50]

Nurcan et al. did a study in Turkey in 200 patients to investigate the clinical value of MPV in coronary atherosclerosis & it's possibility of being an independent risk factor for acute MI. MPV was found to be elevated in MI patients compared with controls ($p<0.001$) &(SAP<0.05) &patients with two($P<0.001$) and three vessel ($p<0.05$) disease. A significant association was seen between MI and higher MPV (≥12fL).[10]

Awad-Elkareem Abass et al in Sudan did a study 103 patients with CAD; and 100 patients with non cardiac chest pain. They found out that Mean Platelet Volume, platelet distribution width and platelet large cell ratio were significantly higher in ACS compared to controls (P-values<0.05).[51]

Abdullah et al. did a study in Kingdom of Saudia Arabia in 2011 to identify to identify diagnostic and prognostic factors for Acute Coronary Syndrome in which Mean Platelet Volume and Platelet Distribution Width were also investigated.A retrospective study of 212 patients with ACS and 49 matched controls. The MPV was significantly larger in MI cases compared to controls (8.99±1.5fL vs 8.38±0.5fL,respectively,$P<0.009$).The MPV was significantly higher in MI cases compared to controls (15.88±1.5fL vs 11.96±1.8fL,respectively,$P<0.001$).[51]

Ugur et al. did a study in 2012 in Turkey in 441 consequtive patients undergoing coronary angiography by measuring platelet indices .there was no statistical difference for platelet count MPV & PDW among the groups .correlation analysis showed a positive association between platelet count and Gensini scoring (Kendalls tau b ,r=0.312,p=0.037,two tailed)&also age (Kendalls tau b,r=0.512,p=0.001,two tailed) in patients with CAD. However there was no significant correlation between Gensini scoring &MPV values in these patients .[8]

MATERIALS AND METHODS

Study design: Observational Study.

Study setting (Exact place where the study is conducted): Department of General Medicine and Department of Cardiology, Sree Mookambika Institute of Medical Sciences, Kulashekharam, Kanyakumari District during the decided study period.

Approximate total duration of the study: 18 months

Number of groups to be studied: 2 groups

Detailed description of the groups:

Group 1-Patients presenting with STEMI, NSTEMI.

Group 2- Age and sex matched patients coming to the hospital with non cardiac chest pain

Sampling:

Sample size of each group: 85

Total sample size of the study: 170

Scientific basis of sample size used in the study:

$$n = \frac{ZS^2[Z_\alpha+Z_\beta]^2}{(M_1-M_2)}$$

M_1=Mean platelet volume in ACS=11.44 (Randheer et al.[10])

M_2=Mean platelet volume in ACS=9.91

S_1=1.23

$S_{2=}$1.27

Z_α=1.64

Z_β=0.84

Power=80%

Sample size=85

Sampling technique used in the study: Convenient sampling

Inclusion criteria:

GROUP 1-

1. Age-35- 75 years.

2. Positive ECG findings.

3. Troponin T positive.

GROUP 2-

1. Age 35-75 years

2. No positive findings in ECG.

3. Troponin T test negative.

Exclusion criteria:

1. Critically ill patients (ACA associated with hepatic failure, renal failure, myeloproliferative disorder or malignancy).

2. Patients having platelet disorder such as thrombocytopenia or thrombocytosis.
3. Patients with any bleeding disorder.
4. Patients with any clotting disorder.
5. Patients on previous anti platelet therapy.
6. Patients on fibrinolytics.
7. Patients on Anti cancer therapy.

Procedure in detail:

After acceptance of the protocol by the ethics committee an informed consent will obtained from those patients diagnosed with ACS presenting in the casualty or Medicine OPD of Sree Mookambika Institute of Medical Sciences who fulfil the criteria of inclusion and exclusion.

History taking:

Profoma is used for documenting age /sex /address / clinical information/symptoms/predisposing factors/and any previous history of treatment.

Collection of samples:

2 ml of blood will be collected in an EDTA container from the patient's medial cubital vein on admission which should be from 6 hours from onset of chest pain.

This sample will be immediately sent to the haematology unit of the Central Lab to obtain the platelet indices by 1) MINDRAY BC5300 & 2) Beckman Coulter Autoanalyser (reagent used: diluent).

BECKMAN COULTER AUTOANALYSER (AU480)

RESULTS & ANALYSIS

SOCIODEMOGRAPHIC CHARACTERISTICS

AGE DISTRIBUTION

The distribution of age in ACS patients ranges from 34 to 75 years. The mean age of study participants were 55.66 years (95% CI is 54.52, 56.68) and a SD of 9.967 years.

The distribution of age in non ACS patients ranges from 34 to 74 years. The mean age of study participants were 56.35 years (95% CI is 54.327, 58.373) and a SD of 9.518 years.

Table 1:Distribution according to age of participants

Age characteristics	ACS	Non ACS
	Value	Value
Minimum	34	34
Maximum	75	74
Mean	55.66	56.35
Standard deviation	9.967	9.518

In ACS patients majority of them were 50-59 years of age group (34.1%), followed by 40-49 years of age group and 60-69 years of age group (27.1%). In non ACS patients majority of them were 60-69 years of age group (40%), followed by 50-59 years of age group (30.6%) and 40-49 years of age group (21.2%).

Table 2:Age distribution in the study population

Age group	ACS		Non ACS	
	Frequency	Percentage	Frequency	Percentage
30-39	5	5.9	5	5.9
40-49	23	27.1	18	21.2
50-59	29	34.1	26	30.6
60-69	23	27.1	34	40
70-79	5	5.9	2	2.4
Total	85	100	85	100

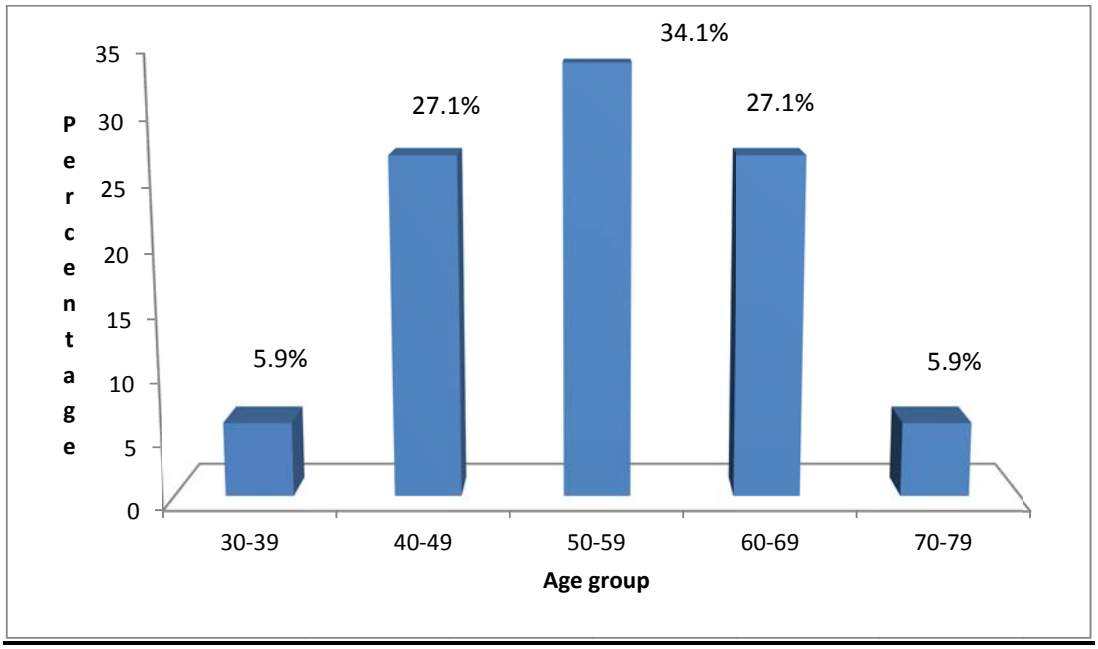


Fig 11:Graph showing the distribution of age group in ACS patients

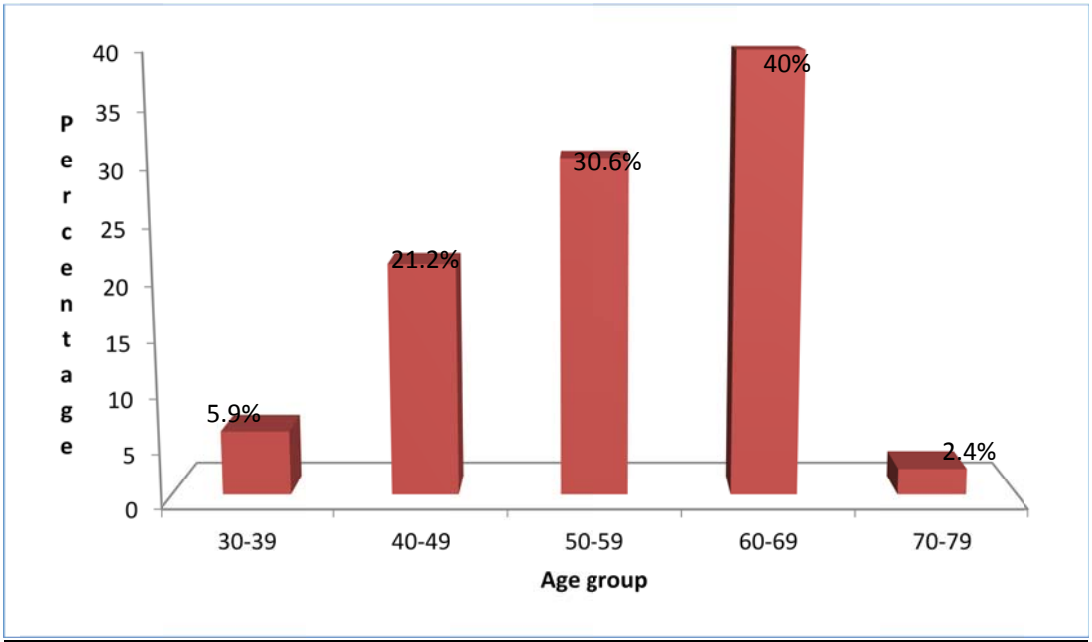


Fig 12:Graph showing the distribution of age group in non ACS patients

GENDER

In ACS patients 61.2% (52) were males and 38.8% (33) were females. In non ACS patients 70.6% (60) were males and 29.4% (25) were females.

Table 3:Distribution of gender

Gender	ACS		Non ACS	
	Frequency	Percentage	Frequency	Percentage
Male	52	61.2	60	70.6
Female	33	38.8	25	29.4
Total	85	100	85	100

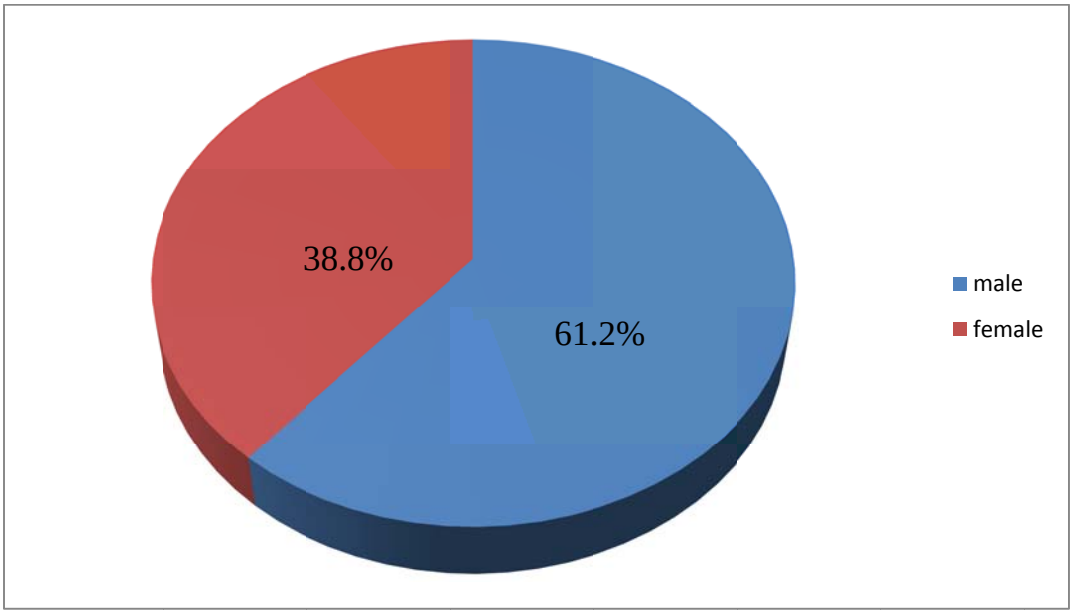


Fig 13:Distribution of gender in ACS positive patients

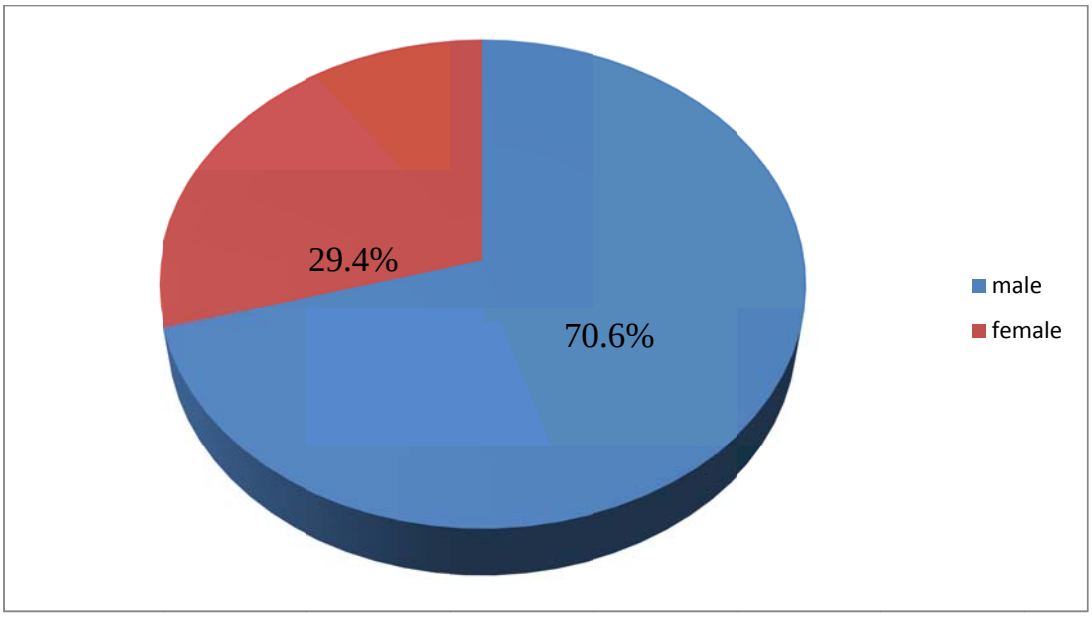


Fig 14:Distribution of gender in non ACS patients

TYPE 2 DIABETES MELLITUS

In ACS patients 56.5% (48) have DM and in non ACS patients 40% (34) have DM

Table 4:Distribution of DM

DM	ACS		Non ACS	
	Frequency	Percentage	Frequency	Percentage
Present	48	56.5	34	40
Not present	37	43.5	51	60
Total	85	100	85	100

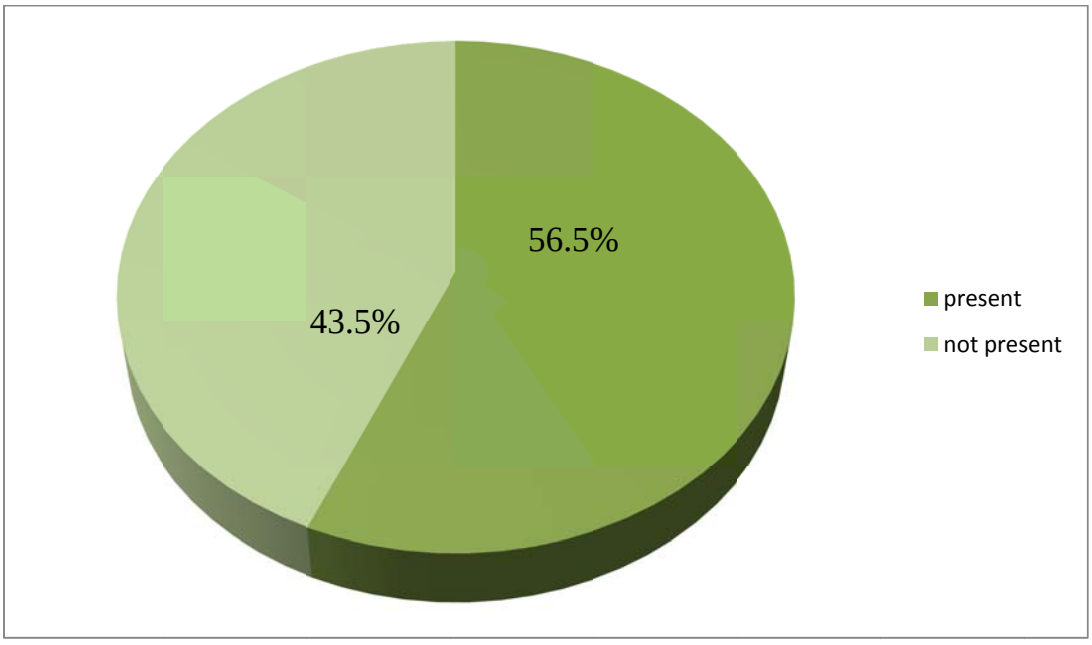


Fig 15:Distribution of DM in ACS patients

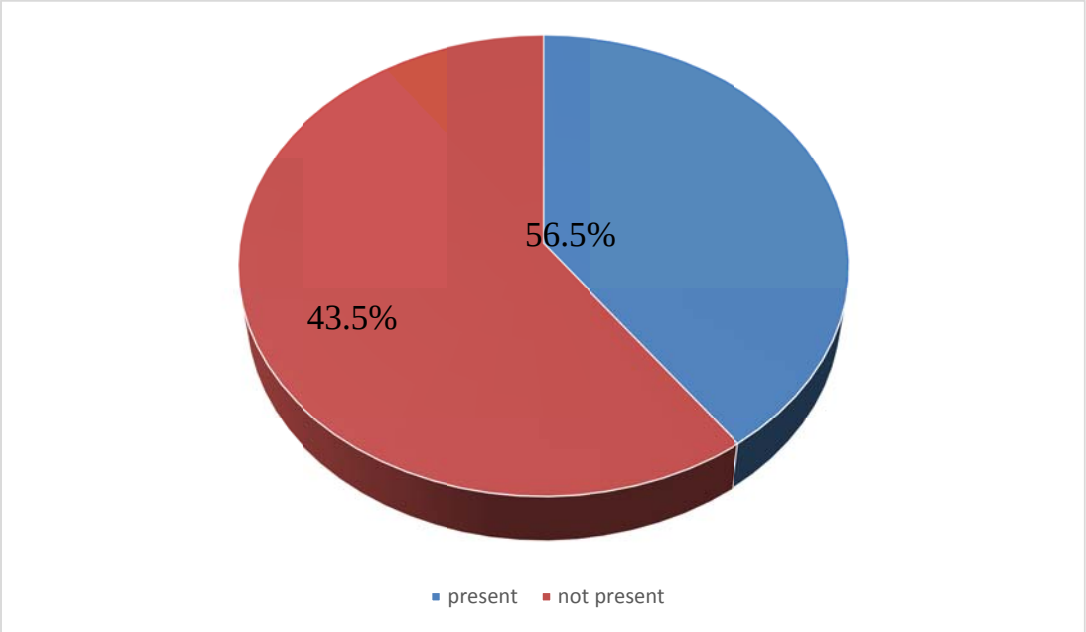


Fig 16:Distribution of DM in non ACS patients

HYPERTENSION

In ACS patients 69.4% (59) were hypertensive's and 30.6% (26) were non hypertensives. In non ACS patients 67.1% (57) were hypertensives and 32.9% (28) were non hypertensives.

Table 5:Distribution of hypertension

Hypertension	ACS		Non ACS	
	Frequency	Percentage	Frequency	Percentage
Present	59	69.4	57	67.1
Not present	26	30.6	28	32.9
Total	85	100	85	100

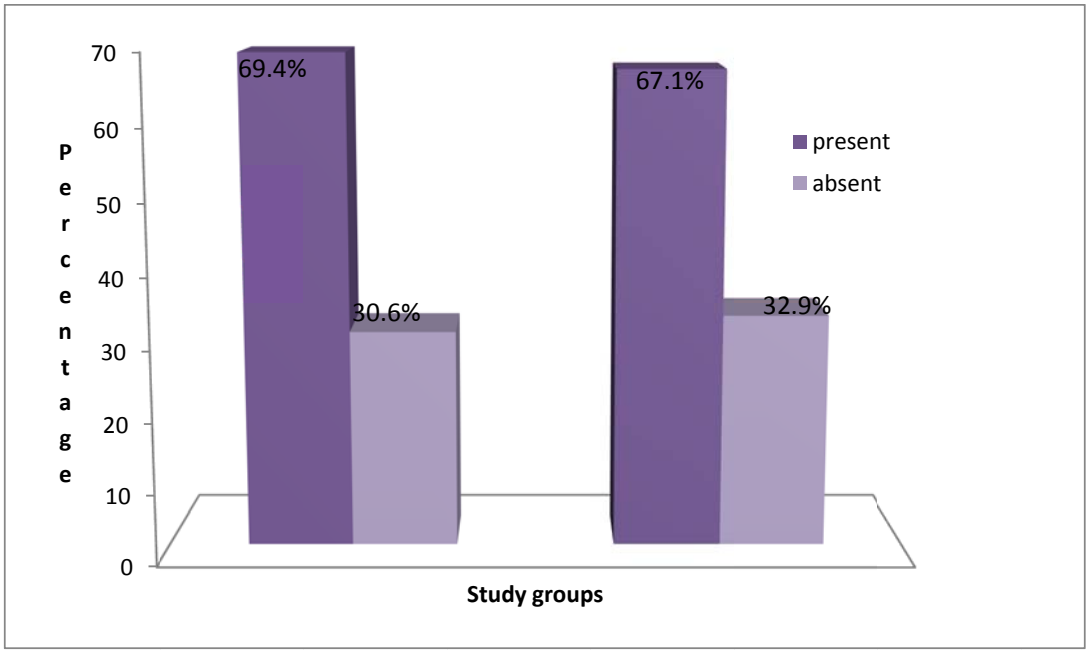


Fig 17:Graph showing the distribution of Hypertension in study groups

SMOKING

In ACS patients 63.5% (54) were smokers and 36.5% (31) were non smokers. In non ACS patients only 35.3% (30) were smokers and 64.7% (55) were non smokers.

Table 6:Distribution of smoking

Smoking	ACS		Non ACS	
	Frequency	Percentage	Frequency	Percentage
Present	54	63.5	30	35.3
Not present	31	36.5	55	64.7
Total	85	100	85	100

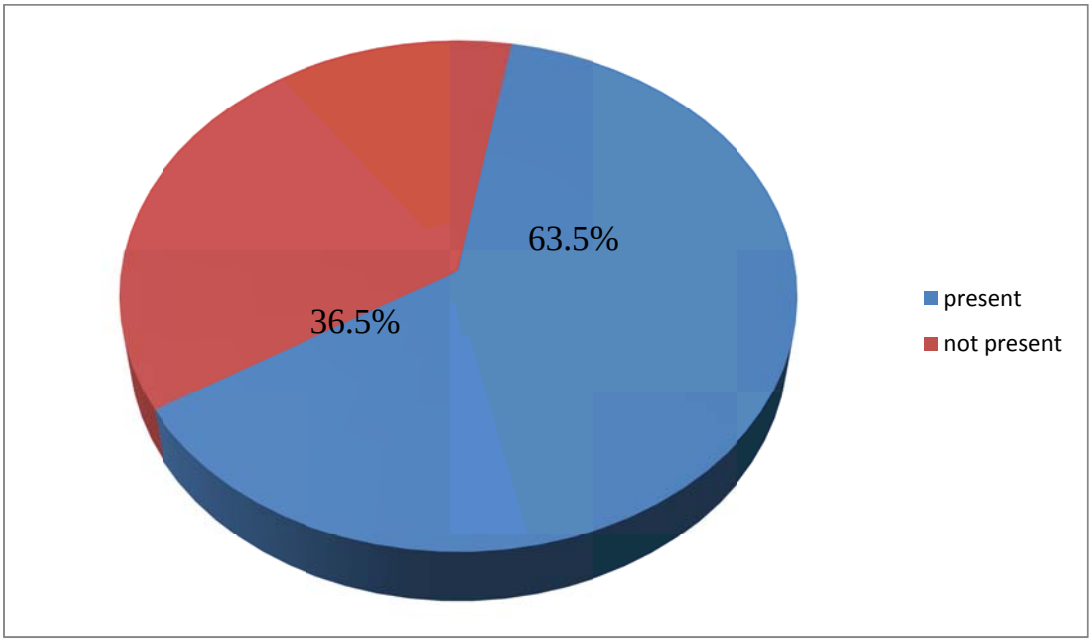


Fig 18:Distribution of smoking in ACS patients

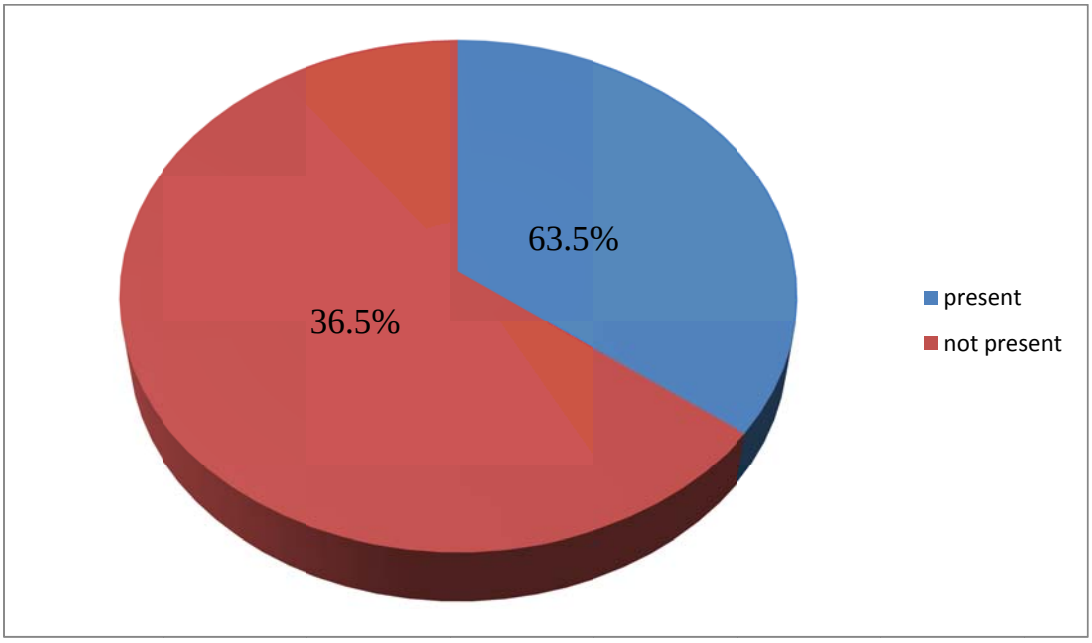


Fig 19:Distribution of smoking in non ACS patients

FAMILY HISTORY

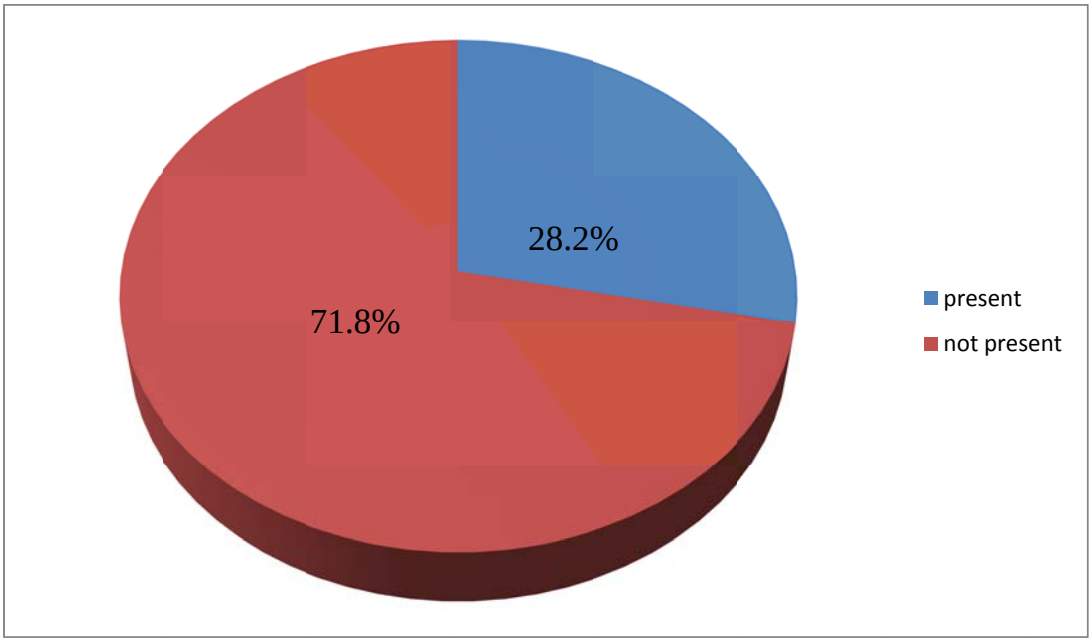


Fig 20:Distribution of family history in ACS patients

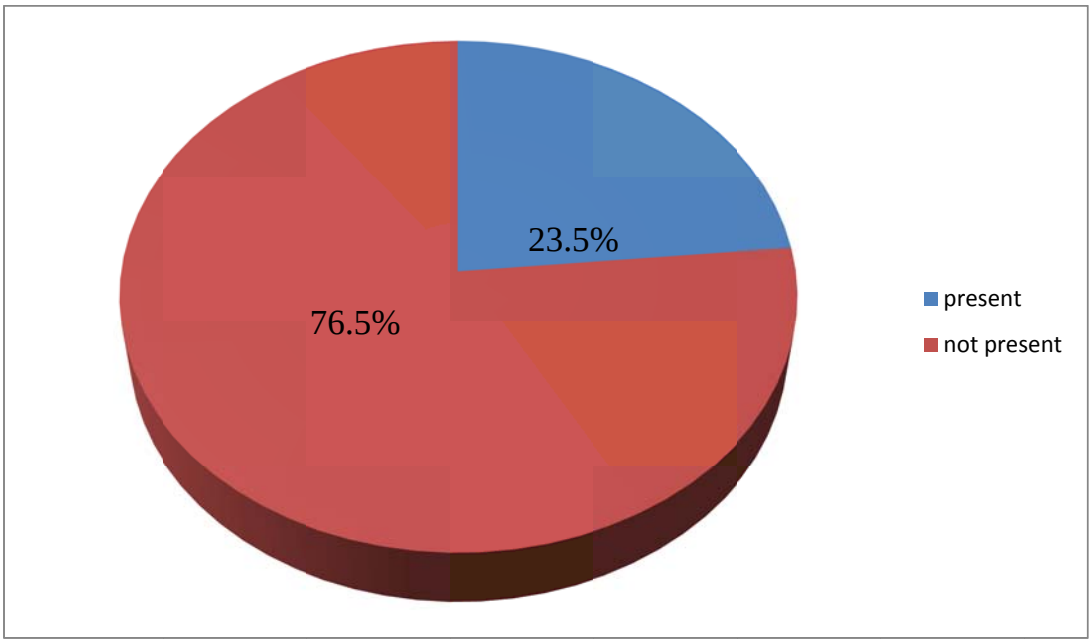


Fig 20:Distribution of family history in non ACS patients

Table 7:Distribution of family history

Family history	ACS		Non ACS	
	Frequency	**Percentage**	**Frequency**	**Percentage**
Present	24	28.2	20	23.5
Not present	61	71.8	65	76.5
Total	85	100	85	100

In ACS patients only 28.2% (24) having family histories and in non ACS patients 23.5% (20) having family histories

TOTAL CHOLESTEROL

The distribution of total cholesterol in ACS patients ranges from 145 to 455. The mean cholesterol level of study participants were 266.33 with a SD of 61.685.

The distribution of total cholesterol in non ACS patients ranges from 100 to 288. The mean cholesterol level of study participants were 167.68 with a SD of 39.402.

Table 8:distribution of total cholesterol 1

Total cholesterol	ACS	Non ACS
	Value	Value
Minimum	145	100
Maximum	455	288
Mean	266.33	167.68
Standard deviation	61.685	39.402

In ACS patients majority of them have high level of cholesterol (55.3%) followed by border line level of cholesterol (29.4%). In non ACS patients majority of them have desirable level of cholesterol (83.5%) followed by border line level of cholesterol (11.8%).

Table 9:Distribution of total cholesterol 2

Total cholesterol	ACS		Non ACS	
	Frequency	Percentage	Frequency	Percentage
Desirable	13	15.3	71	83.5
Border line	25	29.4	10	11.8
High	47	55.3	4	4.7
Total	85	100	85	100

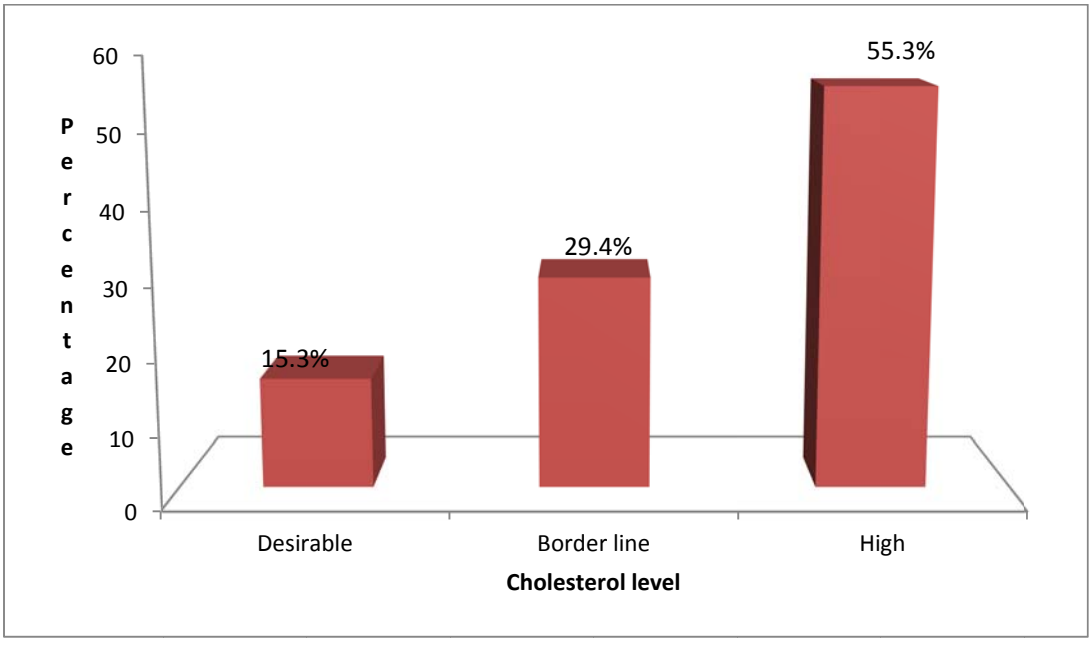


Fig 21:Distribution of total cholesterol in ACS patients

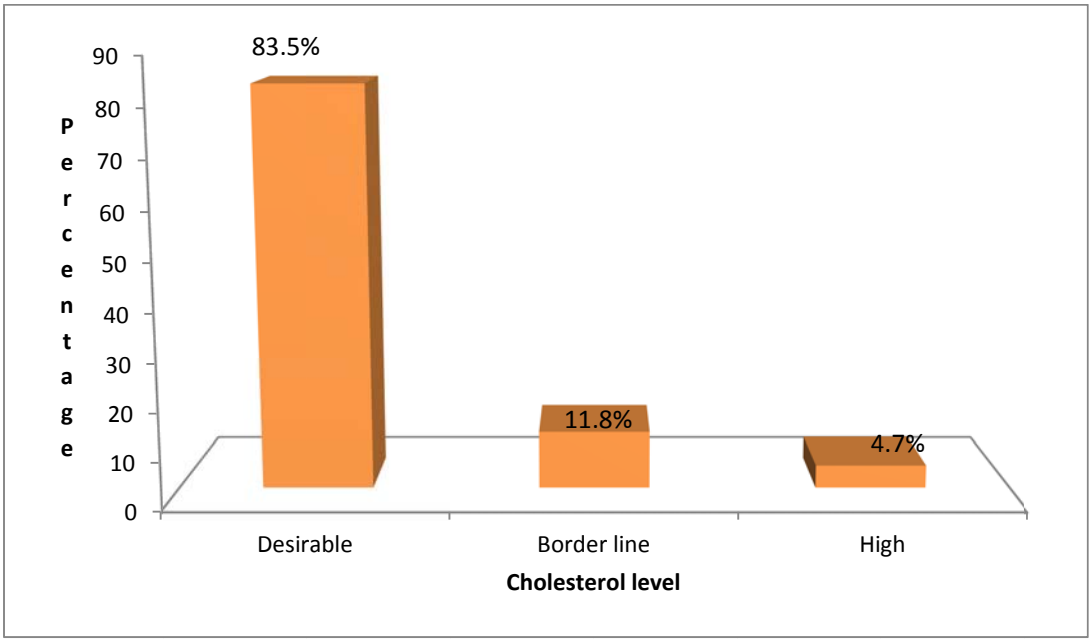


Fig 22:Distribution of total cholesterol in non ACS patients

BMI

The distribution of BMI in ACS patients ranges from 20.2 to 30.4. The mean BMI of study participants were 23.95 with a SD of 2.3. The distribution of BMI in non ACS patients ranges from 17.5 to 27. The mean BMI of study participants were 21.57 with a SD of 1.91.

Table 10:Distribution of BMI

BMI	ACS	Non ACS
	Value	Value
Minimum	20.2	17.5
Maximum	30.4	27
Mean	23.95	21.57
Standard deviation	2.3	1.91

In ACS patients majority of them have normal range of BMI (67%) followed by pre obese (31.8%). In ACS patients majority of them have normal range of BMI (91.8%) followed by 4.7% were under weight.

Table 11:Distribution of BMI

Total cholesterol	ACS		Non ACS	
	Frequency	Percentage	Frequency	Percentage
Under weight	0	0	4	4.7
Normal range	57	67	78	91.8
Pre obese	27	31.8	3	3.5
Obese class I	1	1.2	0	0
Total	85	100	85	100

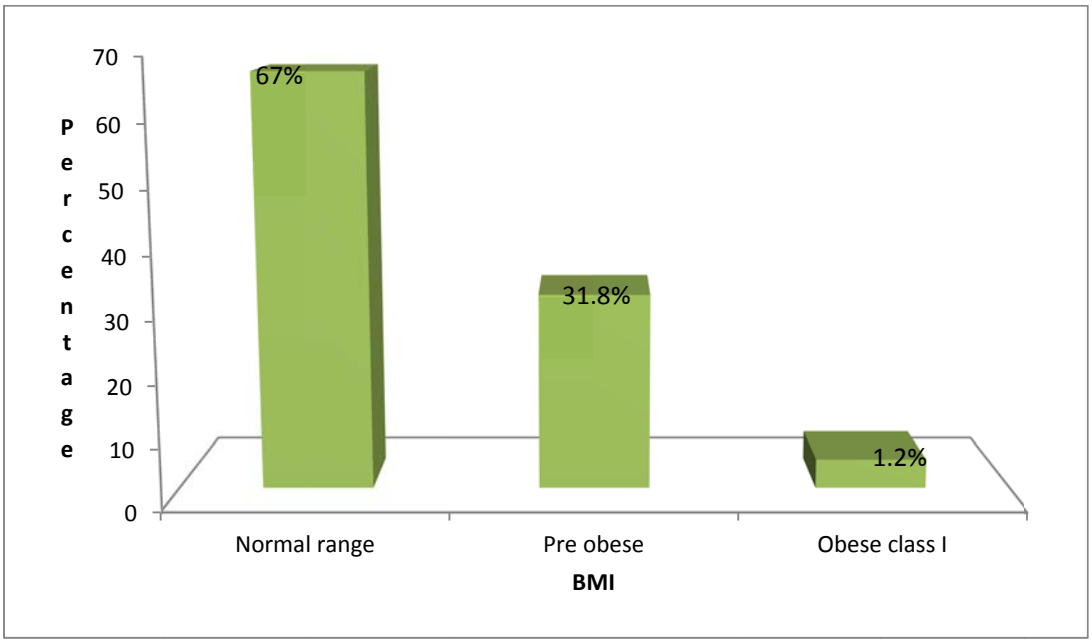


Fig 23 : Distribution of BMI in ACS patients

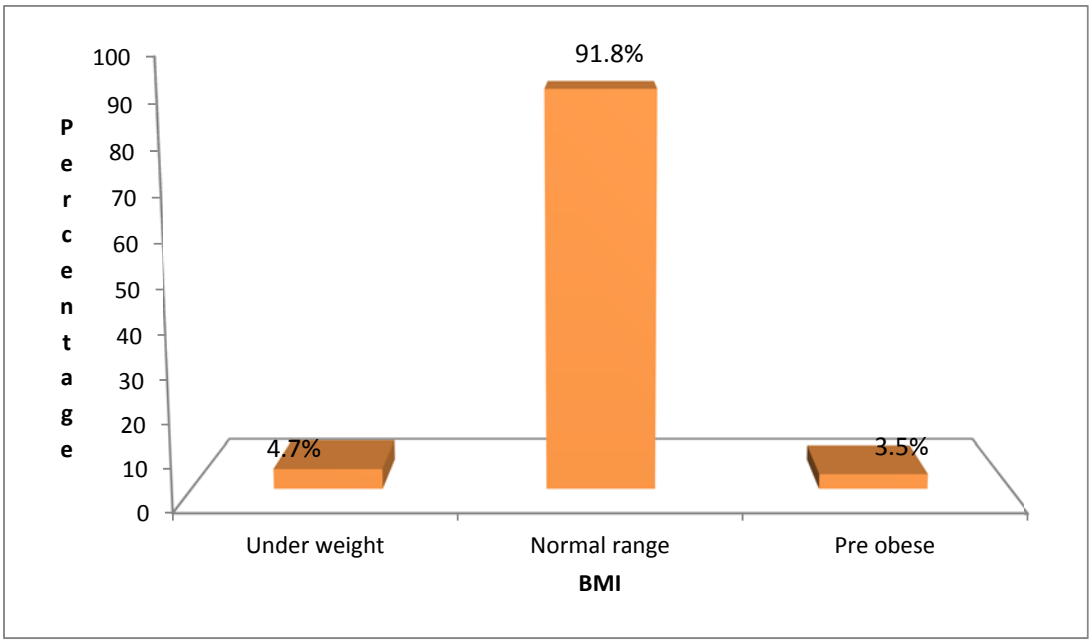


Fig 24 :Distribution of BMI in non ACS patients

MPV

The distribution of MPV in ACS patients ranges from 10.6 to 14. The mean MPV of study participants were 12.468 with a SD of 0.714.

The distribution of MPV in non ACS patients ranges from 9.3 to 14.3. The mean MPV of study participants were 10.636 with a SD of 0.895

Table 12:Distribution of MPV

MPV	ACS	Non ACS
	Value	Value
Minimum	10.6	9.3
Maximum	14	14.3
Mean	12.468	10.636
Standard deviation	0.714	0.895

PDW

The distribution of PDW in ACS patients ranges from 12 to 23. The mean PDW of study participants were 19.134 with a SD of 2.153.

The distribution of PDW in non ACS patients ranges from 9 to 23. The mean PDW of study participants were 13.611with a SD of 2.646.

Table 13:Distribution of PDW

PDW	ACS	Non ACS
	Value	Value
Minimum	12	9
Maximum	23	23
Mean	19.134	13.611
Standard deviation	2.153	2.646

PCT

The distribution of PCT in ACS patients ranges from 1.7 to 3.95. The mean PCT of study participants were 3.1 with a SD of 0.489.

The distribution of PCT in non ACS patients ranges from 1.1 to 3.6. The mean PCT of study participants were 2.19 with a SD of 0.539.

Table 14:Distribution of PCT

PCT	ACS	Non ACS
	Value	Value
Minimum	1.7	1.1
Maximum	3.95	3.6
Mean	3.1	2.19
Standard deviation	0.489	0.539

COMPARISON OF MPV, PDW, PCT BETWEEN ACS AND non ACS PATIENTS

Students 't' test used to compare the mean MPV, PDW, PCT between ACS and non ACS patients. P value less than 0.05 is considered as significant. In this study it is found that there is significant difference in MPV, PDW, PCT in ACS and non ACS patients.

Table :15

Variable	t-value	p-value
MPV	14.745	0.000*
PDW	14.922	0.000*
PCT	11.509	0.000*

Table 16:

	χ^2 value	p value
Age	4.151	0.394
Gender	1.675	0.196
DM	4.618	0.032*
Hypertension	0.109	0.742
Smoking	13.55	0.000*
Family history	0.491	0.484
Total cholesterol	82.731	0.000*
BMI	29.017	0.000*

*p <0.05 is statistically significant

FACTORS ASSOCIATED WITH ACS

Chi-square test or Fisher's Exact test is used to find out the factors associated ACS. p value less than 0.05 is considered as significant. In this study Education DM, smoking, total cholesterol and BMI ($p<0.05$) were associated with ACS.

*p <0.05 is statistically significant

DISCUSSION

The total number of subjects included in my study was 170. Among those 170 subjects, 85 were cases (ACS) and 85 were controls (non ACS).

In our study the age of the study population varies from 35-70 years.The mean age of study participants were 55.66 years (95% CI is 54.52, 56.68) and a SD of 9.967 years.The distribution of age in non ACS patients ranges from 34 to 74 years. The mean age of study participants were 56.35 years (95% CI is 54.327, 58.373) and a SD of 9.518 years. In ACS patients majority of them were 50-59 years of age group (34.1%), followed by 40-49 years of age group and 60-69 years of age group (27.1%). In non ACS patients majority of them were 60-69 years of age group (40%)by 50-59 years of age group (30.6%) .Shukri M Al-Saif , Khalid F. Al Habib, AnharUllah had studied about age and relationship to acute coronary syndrome in a large Saudi population and found out that older patients have higher hospital mortality as they are treated less aggressively.[37]

In our study in those with ACS 61.2% (52) were males and 38.8% (33) were females. In non ACS patients 70.6% (60) were males and 29.4% (25) were females.

In ACS patients 56.5% (48) had type -2 diabetes mellitus and in non ACS patients 40% (34) had type-2 diabetes mellitus. Where as in a study conducted by Laxman Dubey, Sogunuru Guruprasad, Gangapatnam

Subramanyam observed that in group of 223 patients more complex coronary lesions were seen in patients with type 2 diabetes mellitus.[40]

In this study, ACS patients 69.4% (59) were hypertensive's and 30.6% (26) were non hypertensives. In non ACS patients 67.1% (57) were hypertensives and 32.9% (28) were non hypertensives.

In this study, in ACS patients 63.5% (54) were smokers and 36.5% (31) were non smokers. In non ACS patients only 35.3% (30) were smokers and 64.7% (55) were non smokers.in a study conducted by Khaled Hbejan in 1107 cases he found out that Myocardial infarction risk increased with increasing daily number of cigarettes smoked. The risk of an acute myocardial infarction doubled in smokers of 1 to 15 cigarettes a day.[41]

Also the mean cholesterol level of study participants were 266.33 and distribution of total cholesterol in non ACS patients ranges from 100 to 288.In ACS patients majority of them have high level of cholesterol (55.3%).

Whereas, the distribution of BMI in ACS patients ranges from 20.2 to 30.4. The mean BMI of study participants were 23.95 with a SD of 2.3.The distribution of BMI in non ACS patients ranges from 17.5 to 27.There were 27 patients who belonged to the pre obese group and al were in the group of cases. When compared to study done by**Jon Dooley, Anna Marie Chang** in Pennsylvania in about 3946 patients it was observed thatalthough increased levels of obesity were associated with a greater number of cardiac risk factors, there was no difference in 30-day cardiovascular events between those

ofnormal weight and underweight , overweight , obese, or very obese. Those who were underweight were more likely to be readmitted within 30 days, and those who were very obese were less likely to be readmitted within30 days.[42]

The distribution of MPV in ACS patients ranges from 10.6 to 14. The mean MPV of study participants were 12.468 with a SD of 0.714.The distribution of MPV in non ACS patients ranges from 9.3 to 14.3. It was found out there was significant association with MPV and ACS. Similarly in a study by**Kruthika S Patil, S D Karchi** in Banglore have reported that patients with acute coronary syndromes had higher MPV when compared to NCCP group.[43]

The distribution of PDW in ACS patients ranges from 12 to 23. The mean PDW of study participants were 19.134 with a SD of 2.153.The distribution of PDW in non ACS patients ranges from 9 to 23. The mean PDW of study participants were 13.611with a SD of 2.646.The present study showed that there was significant association between Platelet Distribution Width and ACS.A cross sectional study done by **IdarMappangara, Ali AsparMappahya, Sheila Witjaksono**in Indonesia ,there were significantly higher PDW (p=0.047) in STEACS group (13.7±2.0 fL) than in NSTEACS group (12.6±2.3 fL). There were a significant positive correlation between PDW .[44]

The distribution of PCT in ACS patients ranges from 1.7 to 3.95. The distribution of PCT in non ACS patients ranges from 1.1 to 3.6. The mean PCT of study participants were 2.19 with a SD of 0.539.

Whereas in a cross-sectional study conducted by**Mehmet Serkan Cetin, ElifHandeOzcan Cetin, Ahmet Akdi**consisted 565 subjects which classified into three groups:group 1 (168 young patients with STEMI), group 2 (173 non-young patients with STEMI), andgroup 3 (224 age-matched controls with angiographically normal coronary arteries).In Group 1, PDW and PCT were significantly higher than the other groups.[45]

CONCLUSION

- Platelet indices in patients with ACS were significantly increased when compared to the normal population.
- Diabetes, smoking, raised total cholesterol and BMI were also additional risk factors in the development of ACS.
- There is no role of family history in the development of ACS as per my study.
- More males presented with complaints of chest pain and were diagnosed to have ACS compared to females.

SUMMARY

The WHO has drawn attention the fact that coronary artery disease is a modern epidemic more in geriatric population ie, people above 60 years of age. Large increase in coronary artery disease has been projected and now it is the most common cause of death.

Previous data suggests that only 1/3rd of chest pain cases require emergency care and hospitalization but in the absence of segregation of these cases in the beginning, physicians over admit such patients and it burns out the precious resources in the public setup . Further it may reduce the quality of care for those who actually require it.

Platelet indices is a simple and economic laboratory measurement (less costly and can be done when a complete blood count is already requested), I suggest that it might be useful as an assisting rule-out test in conjunction with other conventional biochemical cardiac markers in the early prediction of the risk of ACS in patients admitted to the emergency department.

The study was a hospital based observational study conducted in Sree Mookambika Institute of Medical Sciences, Kulashekharam, KanyaKumari district.

The total number of subjects included in the study was 170.among those 85 were cases (with chest pain diagnosed to have ACS) and the rest were

controls (patients with non cardiac chest pain).In my study the age of the population varies from 35 to 70 years .In my studyThe mean age of study participants with ACS and non ACS was 55.66 years and 56.35 years respectively.In ACS patients 61.2% (52) were males and 38.8% (33) were females. In non ACS patients 70.6% (60) were males and 29.4% (25) were females. Among the cases 54 had the habit of smoking whereas among controls only 30 patients had the habit.In ACS patients 56.5% (48) have diabetes mellitus and in non ACS patients 40% (34) have diabetes mellitus.

Only 24 patients among the cases had a positive family history,similarly only 20 patients had a positive family history in control group also.In those patients who had ACS majority of them have normal range of BMI (67%) followed by pre obese (31.8%). In non ACS patients majority of them have normal range of BMI (91.8%) followed by 4.7% were under weight. High cholesterol levels were also seen to be associated with ACS as 47 people out the cases were found to have high cholesterol levels compared to the controls where 4 subjects had only higher levels of cholesterol.

The mean BMI of those who presented with ACS was 23.95 whereas the mean BMI of patients with non cardiac chest pain was 21.57 .

The mean MPV of study participants who presented with ACSwere 12.468.

While observing the mean MPV of study participants without ACS it was 10.636 .so there was significant correlation between MPV and ACS.

In the case of the next platelet parameter PDW it was found that in patients who presented with ACS the mean value was 19.134.. The mean PDW of study participants were 13.611.Similarly in the case of the plateletcrit the mean PCT of study participants with ACS was 3.1 .The distribution of PCT in non ACS patients ranges from 1.1 to 3.6. The mean PCT of study participants were 2.19 with a SD of 0.539. Hence in this study it was observed that there is significant difference in MPV, PDW, PCT in ACS and non ACS patientsanother observation is thatin this study DM, smoking, total cholesterol and BMI ($p<0.05$) were associated with ACS.

LIMITATIONS

The study group was small, that is, the study group of 150 patients could not be extrapolated to the general population.

Serum MPV, PDW. PCT, and other tests like serum cholesterol was taken only once so their variability as time passed was not studied which made us unable to account for intra individual variability.

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ANNEXURE – I

SREE MOOKAMBIKA INSTITUTE OF MEDICAL SCIENCES

(Kulasekharam (K.K District, TN)-629161, Phone No: 04651-280866, Fax No: 280740)

Institutional Human Ethics Committee (IHEC)

{CDSCO Reg No: ECR/446/Inst/TN/2013}

Ref. No: SMIMS/IHEC/2015/A/35 Date: 17th February 2016

CERTIFICATE

This is to certify that the Research Protocol Ref. No. **SMIMS/IHEC/2015/A/35** entitled "Association Between Platelet Indices and Acute Coronary Syndrome in a Tertiary Care Center-A Comparative Study" submitted by Dr. Aswathi Harikumar, Postgraduate of Department of General Medicine, SMIMS has been approved by the Institutional Human Ethics Committee at its meeting held on22nd December 2015.

17/2/16.

Dr. Rema Menon. N
Member Secretary
Institutional Human Ethics Committee
Professor and HOD of Pharmacology
SMIMS, Kulasekharam (K.K District)
Tamil Nadu-629161

IHEC Date 17/2/2016

[This Institutional Human Ethics Committee is organized and is operating according to the requirements of ICH-GCP/GLP guidelines and requirements of the Amended Schedule-Y of Drugs and Cosmetics Act, 1940 and Rules 1945 of Government of India.]

ANNEXURE – II

LIST OF ABBREVIATIONS USED

- ACS - Acute Coronary Syndrome
- BMI - Body Mass Index
- MPV - Mean Platelet Volume
- PDW - Platelet Distribution Width
- PCT - Plateletcrit
- SPSS - Statistical Packagefor SocialSciences
- CVD - Cardiovascular Disease
- FGF - Fibroblast Growth Factor
- WHO - World Health Organisation
- IHD - Ischaemic Heart Disease.
- DALY - Disability Adjusted Life Years
- LMIC - Low Medium Income Countries
- HIC - High Income Countries
- AMI - Acute Myocardial Infarction
- STEMI - ST Elevation MI
- NSTEMI - Non ST Elevation MI
- NSTE ACS - Non ST Elevation Acute Coronarysyndrome
- UA - Unstable angina
- TIA - Transient Ischaemic Attack
- LDL - Low Density Lipoprotein
- ECG - Electrocardiography

- LBBB - Left Bundle Branch Block
- VWF - Von Willebrands Factor
- EGF - Epidermal Growth Factor
- SD - Standard Deviation
- DM - Diabetes Mellitus
- UFH - Unfractionated Heparin
- LMWH - Low Molecular Weight Heparin
- PCI - Percutaneous Coronary Intervention
- NTG - Nitroglycerin
- NSAID - Non Steroidal Anti inflammatory Drugs\
- ACE - Acetyl Cholinesterase
- ARB - Angiotensin2 receptor Blocker
- CCU - Coronary Care Unit
- ACC/AHA - American College Cardiology/American Heart Association

ANNEXURE – III

CONSENT FORM

PART 1 OF 2

INFORMATION FOR PARTICIPANTS OF THE STUDY

Dear Participants,

We welcome you and thank you for your keen interest in participation in this research project. Before you participate in this study, it is important for you to understand why this research is being carried out. This form will provide you all the relevant details of this research. It will explain the nature, the purpose, the benefits, the risks, the discomforts, the precautions and the information about how this project will be carried out. It is important that you read and understand the contents of the form carefully. This form may contain certain scientific terms and hence, if you have any doubts or if you want more information, you are free to ask the study personnel or the contact person mentioned below before you give your consent and also at any time during the entire course of the project.

1. Name of the Principal Investigator : Dr.AswathiHarikumar
General Medicine Post Graduate
Department of General Medicine
SreeMookambika Institute of Medical Sciences

2. Name of the Guide : Dr. Kaniraj Peter
HOD,Professor,
Department of General Medicine
SreeMookambika Institute of Medical Science

3. Name of the Co-Guide	**:**	Dr. Ajay kumar Professor Department of Cardiology, SreeMookambika Institute of Medical Sciences
4. Institute	**:**	SreeMookambika Institute of Medical sciences, Kulashekharam, Kanyakumari district-629161 Tamilnadu

5. Title of the study:

ASSOCIATION BETWEEN PLATELET INDICES AND ACUTE CORONARY SYNDROME IN A TERTIARY CARE CENTRE –A COMPARATIVE STUDY

1. Background information:

Acute Coronary syndrome manifests as stable angina pectoris ,unstable angina pectoris, acute myocardial ishcaemia (STEMI and NSTEMI) which are the most common causes of morbidity and mortality .In this scenario platelets play an important role in the pathogenesis of Acute Coronary syndrome. The present cardiac markers are not sufficiently sensitive at an early stage of ACS. That's why an early reliable marker such as platelet indices is needed for the accurate diagnosis of ACS.

7. Aims and Objectives:

To find out and compare the values of platelet indices between ACS and non ACS patients.

8. Scientific justification of the study:

Previous data suggest that only one-fifth of chest pain cases require emergency care and hospitalization but in the absence of segregation of these cases at he beginning physicians tend to overadmit such patients. It burns out the precious resources of resource poor public set up. Thus it will reduce the quality of care of those who actually require it .Moreover, a study of this topic has not been performed in the Kanyakumari district of Tamilnadu.

9. Procedure for the study:

The study is to be carried out at SreeMookambika Institute of Medical Sciences. Relavant clinical and demographic data will be obtained from the patient.

Will document the age/sex/address/clinical information/symptoms/. Predisposing factors and any previous history of treatment.

Blood sample will be collected from the patient on admission which should be 6 hours from the onset of chest pain.

This sample will be immediately sent toHaematology unit of the Central lab to obtain the platelet indices by (i)MindrayBC and(ii) Beckman Coulter Autoanalyzer and reagent used is diluent.

10. Expected risks for the participants: No risk

11. Expected benefits of research for the participants:

These markers can be used to detect an impending major vascular event of Acute Coronary Syndrome and early anti-platelet therapy can be initiated early .

12. Maintenance of Confidentiality: All data collected for the study will be maintained confidentially and would reflect on general statistical analysis only,would not reveal any personal details.

13. Why have I been chosen to be in this study?

1. You have been found to have fulfilled the inclusion and exclusion criteria of selection.
2. You are ready to give consent.

14. How many people will be in the study? 170

15. Agreement of Compensation to the participants (In case of a study related injury): NA

16. Anticipated prorated payment, if any, to the Participant (s) of the study:NA

17. Can I withdraw from the study at any time during the study period: Yes

18. If there is any new findings/ information, would I be informed? Yes

19. Expected duration of the Participant's participation in the study :1 visit

20. Any other pertinent information: No

21. Whom do I contact for further information? Dr.AswathiHarikumar

For any study related queries, you are free to contact

Dr Aswathi Harikumar
General Medicine Post Graduate
Department of General Medicine
SreeMookambika Institute of Medical Sciences
Mobile No. 9585953080
aswathi.harikumar@gmail.com

Place:

Signature of Principal Investigator

Date:

Signature of the Participant

CONSENT FORM

PART 2 OF 2

PARTICIPANTS CONSENT FORM

The details of the study have been explained to me in writing and the details have been fully explained to me. I am aware that the results of the study may not be directly beneficial to me but will help in the advancement of medical sciences. I confirm that I have understood the study and had the opportunity to ask questions. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). I have been given an information sheet giving details of the study. I fully consent to participate in the study titled **'Association between platelet indices and Acute Coronary Syndrome in a tertiary care centre –A comparative study'**

Serial no/Reference no:

Name of the Participant: **Address of the Participant:**

Contact number of the Participant:

Signature/Thumb impression of the participant/Legal guardian

Date: **Witnesses:**

Place 1.

2.

ANNEXURE – IV

Date: SL.NO

Place:

CASE RECORD FORM

AGE: GENDER:

OCCUPATION:

SMOKER: ALCOHOLIC:

HYPERTENSION: DIABETIC:

FAMILY HISTORY:

ANTI- PLATELET THERAPY: BLEEDING OR CLOTTING DISORDERS:

MALIGNANCY: MYELOPROLIFERATIVE DISORDERS:

ON EXAMINATION

WEIGHT: HEIGHT:

PR: BP:

INVESTIGATIONS

CBC:

MPV: PDW : PCT:

TOTAL CHOLESTEROL:

ECG:

TROPONIN T:

ANNEXURE – V

MASTER CHART

AGE	gender	DM	HTN	smoking	total cho	BMI	familyh/o	ECG	trop t	MPV	PDW	PCT
45	1	1	1	1	150	25.4	2	1	1	13.7	17	2.05
46	1	2	2	2	300	24	2	2	1	12	20	2.06
50	1	2	1	1	245	21	2	3	1	12.9	12	3
54	2	2	1	2	300	26	2	2	1	11.9	13	2.9
60	2	1	1	2	134	20	2	3	2	9.7	12	1.5
45	1	1	2	2	345	27.6	2	1	1	12	22	2.9
56	1	1	2	1	230	23.2	1	2	1	12.3	21	3.12
64	1	2	2	2	245	23	1	1	1	12.5	20	2.88
62	2	2	2	2	234	20	2	3	2	10.3	14	1.2
49	2	2	1	2	345	27.6	2	1	1	12.8	19	3.01
50	1	2	1	1	321	25	2	2	1	11.8	18	2.9
67	1	2	1	1	234	24.6	2	2	1	11.8	21	3.5
58	1	1	1	1	347	22	2	1	1	13.4	22	3.2
49	1	1	1	1	277	26	2	3	2	10.5	19	1.6
67	1	1	1	1	255	22.6	2	2	1	13.2	13	1.7
66	1	2	1	1	320	25	2	2	1	11.7	18	3.4
55	2	2	1	2	145	20	2	3	2	11.5	9	1.4
50	1	2	2	2	200	21.7	1	2	1	11.3	19.5	2.2
47	1	2	1	2	400	27.5	1	1	1	11.8	20.5	3.5
66	2	2	1	2	311	24.7	1	1	1	12.4	21	3.9

41	1	2	1	1	345	23.4	1	2	1	12.2	19	3.8
53	1	1	1	1	234	20.8	1	1	1	11.7	13	3.7
58	1	1	1	1	256	22	1	3	2	10.4	14	2.1
64	2	2	2	2	237	21	2	2	1	13.4	20	2.6
63	2	2	2	2	211	23.8	2	3	1	13.2	18	2.8
55	2	2	2	2	222	21	2	2	1	11.5	18.5	3
44	1	1	2	2	331	26.2	2	1	1	12.5	17.6	2.95
45	1	1	1	1	123	20.1	2	3	2	10.3	15	2.1
39	1	1	1	2	222	21.2	2	3	2	11.3	16	1.3
45	1	1	1	1	209	19.6	2	3	2	10.9	19	1.8
66	2	1	1	2	165	20.7	2	3	2	10	16	2.5
66	1	1	1	1	145	23	2	2	1	13.2	19	2.05
59	1	2	1	1	165	19	2	3	2	12	16	2.95
45	1	2	2	1	300	21	2	2	1	11.5	20	3.95
47	2	1	2	2	241	23.6	1	2	1	12.9	21	3.1
68	2	2	2	2	254	22.3	1	3	2	13.4	23	3.3
62	1	2	1	2	266	24.4	2	1	1	12.7	20.5	2.99
64	1	2	1	2	288	22	2	3	2	11.5	11	2.6
53	1	1	1	2	122	18.7	2	3	2	11.4	12	2.88
50	1	1	1	2	156	19.7	2	3	2	11.3	13.5	2.7
39	2	1	1	2	170	21	2	3	2	10.3	14.6	2.6
45	1	1	2	1	190	20.3	2	3	2	11.1	13	2.2
65	1	2	1	1	187	20.9	2	3	2	10.4	14	2.4
40	1	2	2	2	145	19.2	2	3	2	10.3	15.6	2.2
47	2	2	1	2	300	22.3	2	2	1	12.3	19.6	3.7

44	2	2	2	2	320	23.6	2	1	1	12.5	20	3.8
54	1	2	1	2	200	22.6	2	3	2	9.7	15	2.2
45	1	2	2	2	215	20.1	2	3	2	9.8	12	2.2
67	1	1	1	1	231	21.8	2	2	1	14	18.5	3.2
70	2	1	2	2	300	24.6	2	2	1	12.4	17	3.1
38	1	1	1	2	211	22.3	1	2	1	13.4	19	3.9
67	1	1	1	1	165	20.4	1	2	1	11.6	17	3.7
56	2	1	1	2	159	20.8	1	3	2	9.9	13	2.6
34	1	1	1	2	288	25.9	1	1	1	11.4	18.5	2.7
65	2	1	1	2	111	18.7	1	3	2	10	14	2
66	1	1	2	2	133	23.4	1	3	2	10.1	16	1.9
34	1	1	2	1	155	21.5	2	3	2	11.1	12.6	1.3
45	1	1	2	2	122	23	2	3	2	11.5	17	1.1
65	2	2	1	2	176	22	2	2	1	12.6	17	1.9
74	1	1	1	2	156	23	2	3	2	11.5	15	1.2
54	1	2	1	1	123	21	2	3	2	11.7	14	1.9
55	2	1	1	2	144	24	2	3	2	11.3	11	1.8
44	2	2	1	2	211	23	2	2	1	12.2	17.5	3.2
34	1	1	1	1	222	22	2	3	2	10.5	14	2.2
59	1	2	1	1	234	25.6	2	1	1	12.8	17	2.7
71	1	1	2	2	256	23	2	2	1	10.6	15	2.2
37	2	2	2	2	300	27.7	2	1	1	12.9	18	3.2
65	1	1	2	2	344	25.7	2	2	1	13.11	18.7	3.1
57	1	2	2	1	455	26	2	1	1	12.9	20	3.3
69	1	1	1	1	344	24.5	1	2	1	11.9	18	2.9

59	1	1	1	1	277	23	2	1	1	12	17	2.56
67	2	1	1	2	344	26	2	2	1	12	19	2.9
45	2	2	1	2	233	23	2	2	1	13.5	18.5	3.1
67	1	2	1	2	366	24.5	2	2	1	13.6	17	3.2
55	1	1	1	2	233	22	2	2	1	12.6	21	3.3
58	1	2	1	2	256	23	2	1	1	11.7	18.5	3.4
54	2	1	1	2	333	25.5	2	1	1	12.8	17	3.5
45	1	2	2	2	216	23	1	1	1	12.4	19	2.2
43	1	1	2	2	219	22	1	3	2	11.3	13	2.5
49	1	2	2	1	333	24	1	1	1	11.4	16.7	3.5
50	1	1	2	1	124	19.7	1	3	2	9.5	10	2.1
53	1	2	1	1	156	20.2	2	3	2	9.8	10.5	2.4
64	2	1	1	2	176	20.8	1	3	2	9.5	11	2.05
67	2	1	1	2	145	19.4	2	3	2	10.8	16	1.7
55	1	1	1	2	123	21	2	3	2	10.3	19	1.8
75	1	2	1	2	234	22	2	2	1	12.3	18	3.2
56	1	2	1	2	125	20	2	3	2	10.5	15	2.5
66	1	2	2	1	100	23.3	2	3	2	10.6	14	2.3
54	1	2	2	1	167	23	2	3	2	10.5	17	2.2
58	2	2	2	2	176	21	2	3	2	10.3	16	2.1
68	2	1	2	2	123	19.8	2	3	2	9.3	17	1.7
45	2	1	2	2	145	18.4	2	3	2	11.2	12	1.8
49	1	1	1	2	198	19.3	2	3	2	11.9	15	1.33
59	1	2	1	2	187	20.2	2	2	1	11.9	19	2.7
60	1	2	1	2	176	23.9	2	3	2	10.2	18.5	2.3

61	1	2	1	2	156	24	2	3	2	9.8	15	2.8
66	1	2	1	1	144	24.4	2	3	2	9.9	11	2.8
68	1	1	1	1	199	21.1	2	3	2	10.9	12	2.1
46	1	1	1	1	188	22	2	3	2	11.4	15	2.9
75	1	1	1	1	233	20.5	2	2	1	12.1	19	3.3
49	2	1	2	2	266	23	1	2	1	14	17	3.1
56	1	1	1	1	254	28	1	2	1	13.5	20	3.5
57	2	2	2	2	188	20.9	1	2	1	12	21	3.8
67	2	2	1	2	155	23	1	3	2	10.3	14	2.7
64	1	2	2	1	177	21.8	1	3	2	11.9	12	2.6
62	1	2	1	2	233	23	1	2	1	13.12	19	3.1
60	1	2	2	2	111	21.9	2	3	2	9.9	16	2.7
50	2	2	1	2	109	20.3	2	3	2	10.3	14	2.1
67	1	1	1	2	200	21.1	2	3	2	10	10	1.9
45	1	1	1	2	277	20.9	2	2	1	13.2	19.5	3.6
55	1	1	1	1	234	29.4	2	1	1	12.7	20	3.2
44	2	1	1	2	344	27.4	2	2	1	12.12	22	3.21
36	2	1	1	2	211	23.3	2	1	1	13.4	21	3.6
46	1	2	1	1	222	22.2	2	3	2	14.3	17.7	3.6
45	1	2	1	1	122	21.9	2	3	2	12	16	1.9
70	1	2	1	2	134	23	2	3	2	11.4	12	1.88
67	2	2	1	2	156	21.8	2	3	2	11.3	13	2.44
68	1	2	1	2	176	22.7	2	3	2	10.2	13	2.56
65	1	2	2	2	144	21.7	2	3	2	9.5	12	2.5
56	1	2	2	2	155	23.7	2	3	2	9.5	16	2.33

57	2	1	1	2	187	24	2	2	1	12.3	20	3.6
58	2	1	1	2	197	21.9	1	2	1	11.8	22	3.2
59	1	1	1	1	197	27	1	2	1	11.8	21	3.2
46	1	1	1	1	123	23.9	1	3	2	9.9	12	2.2
56	1	2	1	1	145	21.8	2	3	2	9.5	13	2.4
54	2	2	1	2	154	22.8	2	3	2	10.5	11	2.77
53	1	2	1	1	222	23.1	2	2	1	13	19	3.9
65	2	2	1	2	155	22.7	2	3	2	11.3	11	2.99
64	1	2	1	1	211	27	2	3	2	11.2	10	2.11
48	1	1	2	2	200	23.8	2	2	1	11.7	19.5	2.95
56	1	1	2	1	166	24.9	2	3	2	10.9	11	2.1
67	1	1	2	2	156	18.4	2	3	2	9.9	10	1.9
68	1	1	2	1	198	19.4	1	3	2	9.9	15	2.37
66	2	1	1	2	178	20.5	1	3	2	9.8	12	2.75
45	2	2	1	2	109	21	1	3	2	11.4	13	1.23
55	2	1	1	2	177	24	1	3	2	11.4	11	1.4
44	1	2	1	1	234	23.6	2	1	1	11.8	19	2.79
65	1	2	1	1	298	25.5	2	1	1	11.4	20	2.7
58	2	2	1	2	222	30.4	2	2	1	11.9	22	3.45
67	2	1	1	2	322	27.7	2	2	1	12.5	22	3.7
45	2	1	1	2	377	24.9	2	2	1	12.2	20.5	3.55
56	1	1	1	2	344	23	2	2	1	12.6	22	3.2
48	1	2	1	2	222	24.4	2	3	2	10.8	14	2.05
59	1	1	2	2	111	22.2	2	3	2	10.8	12	2.23
39	2	2	2	2	211	23.3	2	3	2	11.1	9	2.9

56	2	1	2	2	266	21.9	2	2	1	12.8	18	2.5
67	2	2	2	2	333	24.4	2	1	1	13	19	2.99
68	2	1	2	2	156	26.6	1	3	2	11.3	11	3.5
53	2	2	2	2	166	20.8	1	1	1	12.6	19	2.87
54	2	1	1	2	155	22.4	1	3	2	9.5	14	2.13
64	1	2	1	1	132	21	1	3	2	9.6	14	2.1
60	1	2	1	1	176	18.5	2	3	2	9.6	16	2.9
62	1	2	1	1	198	19.5	2	3	2	9.6	13	1.76
56	1	1	1	1	176	17.5	2	3	2	9.5	9	1.95
59	1	1	1	2	187	20.1	2	3	2	11.3	10	2.55
66	1	2	1	2	155	22.4	1	3	2	10.3	13	1.1
45	1	2	1	2	154	23.8	1	3	2	9.5	16	1.55
56	1	1	1	2	344	21.1	1	1	1	11.5	22	3.12
67	2	2	1	2	238	25.5	1	2	1	13.5	21	3.2
75	2	2	1	2	200	25	1	2	1	13.2	20.8	3.56
47	2	1	1	2	276	28	2	2	1	12.5	21	3.44
68	1	2	1	1	265	26.6	2	2	1	13.5	21	3.11
67	1	1	1	1	230	21.8	2	1	1	12.8	23	2.99
39	1	2	1	1	300	25.5	2	1	1	12	20	3.22
49	1	1	1	1	231	22.9	2	2	1	11.8	19	3.65
59	1	1	2	1	199	22.9	2	3	2	11.5	10	2.4
66	1	1	2	2	176	21.1	2	3	2	10.9	11	2.85
55	2	1	2	2	300	26.9	2	1	1	12.7	22	2.77
56	2	2	1	2	222	20.5	2	1	1	13.7	20	2.6

AGE	gender	DM	HTN	smoking	total cho	BMI	familyh/o	ECG	trop t	MPV	PDW	PCT
45	1	1	1	1	150	25.4	2	1	1	13.7	17	2.05
46	1	2	2	2	300	24	2	2	1	12	20	2.06
50	1	2	1	1	245	21	2	3	1	12.9	12	3
54	2	2	1	2	300	26	2	2	1	11.9	13	2.9
60	2	1	1	2	134	20	2	3	2	9.7	12	1.5
45	1	1	2	2	345	27.6	2	1	1	12	22	2.9
56	1	1	2	1	230	23.2	1	2	1	12.3	21	3.12
64	1	2	2	2	245	23	1	1	1	12.5	20	2.88
62	2	2	2	2	234	20	2	3	2	10.3	14	1.2
49	2	2	1	2	345	27.6	2	1	1	12.8	19	3.01
50	1	2	1	1	321	25	2	2	1	11.8	18	2.9
67	1	2	1	1	234	24.6	2	2	1	11.8	21	3.5
58	1	1	1	1	347	22	2	1	1	13.4	22	3.2
49	1	1	1	1	277	26	2	3	2	10.5	19	1.6
67	1	1	1	1	255	22.6	2	2	1	13.2	13	1.7
66	1	2	1	1	320	25	2	2	1	11.7	18	3.4
55	2	2	1	2	145	20	2	3	2	11.5	9	1.4
50	1	2	2	2	200	21.7	1	2	1	11.3	19.5	2.2
47	1	2	1	2	400	27.5	1	1	1	11.8	20.5	3.5
66	2	2	1	2	311	24.7	1	1	1	12.4	21	3.9
41	1	2	1	1	345	23.4	1	2	1	12.2	19	3.8
53	1	1	1	1	234	20.8	1	1	1	11.7	13	3.7
58	1	1	1	1	256	22	1	3	2	10.4	14	2.1
64	2	2	2	2	237	21	2	2	1	13.4	20	2.6
63	2	2	2	2	211	23.8	2	3	1	13.2	18	2.8
55	2	2	2	2	222	21	2	2	1	11.5	18.5	3
44	1	1	2	2	331	26.2	2	1	1	12.5	17.6	2.95
45	1	1	1	1	123	20.1	2	3	2	10.3	15	2.1

39	1	1	1	2	222	21.2	2	3	2	11.3	16	1.3
45	1	1	1	1	209	19.6	2	3	2	10.9	19	1.8
66	2	1	1	2	165	20.7	2	3	2	10	16	2.5
66	1	1	1	1	145	23	2	2	1	13.2	19	2.05
59	1	2	1	1	165	19	2	3	2	12	16	2.95
45	1	2	2	1	300	21	2	2	1	11.5	20	3.95
47	2	1	2	2	241	23.6	1	2	1	12.9	21	3.1
68	2	2	2	2	254	22.3	1	3	2	13.4	23	3.3
62	1	2	1	2	266	24.4	2	1	1	12.7	20.5	2.99
64	1	2	1	2	288	22	2	3	2	11.5	11	2.6
53	1	1	1	2	122	18.7	2	3	2	11.4	12	2.88
50	1	1	1	2	156	19.7	2	3	2	11.3	13.5	2.7
39	2	1	1	2	170	21	2	3	2	10.3	14.6	2.6
45	1	1	2	1	190	20.3	2	3	2	11.1	13	2.2
65	1	2	1	1	187	20.9	2	3	2	10.4	14	2.4
40	1	2	2	2	145	19.2	2	3	2	10.3	15.6	2.2
47	2	2	1	2	300	22.3	2	2	1	12.3	19.6	3.7
44	2	2	2	2	320	23.6	2	1	1	12.5	20	3.8
54	1	2	1	2	200	22.6	2	3	2	9.7	15	2.2
45	1	2	2	2	215	20.1	2	3	2	9.8	12	2.2
67	1	1	1	1	231	21.8	2	2	1	14	18.5	3.2
70	2	1	2	2	300	24.6	2	2	1	12.4	17	3.1
38	1	1	1	2	211	22.3	1	2	1	13.4	19	3.9
67	1	1	1	1	165	20.4	1	2	1	11.6	17	3.7
56	2	1	1	2	159	20.8	1	3	2	9.9	13	2.6
34	1	1	1	2	288	25.9	1	1	1	11.4	18.5	2.7
65	2	1	1	2	111	18.7	1	3	2	10	14	2
66	1	1	2	2	133	23.4	1	3	2	10.1	16	1.9
34	1	1	2	1	155	21.5	2	3	2	11.1	12.6	1.3

45	1	1	2	2	122	23	2	3	2	11.5	17	1.1
65	2	2	1	2	176	22	2	2	1	12.6	17	1.9
74	1	1	1	2	156	23	2	3	2	11.5	15	1.2
54	1	2	1	1	123	21	2	3	2	11.7	14	1.9
55	2	1	1	2	144	24	2	3	2	11.3	11	1.8
44	2	2	1	2	211	23	2	2	1	12.2	17.5	3.2
34	1	1	1	1	222	22	2	3	2	10.5	14	2.2
59	1	2	1	1	234	25.6	2	1	1	12.8	17	2.7
71	1	1	2	2	256	23	2	2	1	10.6	15	2.2
37	2	2	2	2	300	27.7	2	1	1	12.9	18	3.2
65	1	1	2	2	344	25.7	2	2	1	13.11	18.7	3.1
57	1	2	2	1	455	26	2	1	1	12.9	20	3.3
69	1	1	1	1	344	24.5	1	2	1	11.9	18	2.9
59	1	1	1	1	277	23	2	1	1	12	17	2.56
67	2	1	1	2	344	26	2	2	1	12	19	2.9
45	2	2	1	2	233	23	2	2	1	13.5	18.5	3.1
67	1	2	1	2	366	24.5	2	2	1	13.6	17	3.2
55	1	1	1	2	233	22	2	2	1	12.6	21	3.3
58	1	2	1	2	256	23	2	1	1	11.7	18.5	3.4
54	2	1	1	2	333	25.5	2	1	1	12.8	17	3.5
45	1	2	2	2	216	23	1	1	1	12.4	19	2.2
43	1	1	2	2	219	22	1	3	2	11.3	13	2.5
49	1	2	2	1	333	24	1	1	1	11.4	16.7	3.5
50	1	1	2	1	124	19.7	1	3	2	9.5	10	2.1
53	1	2	1	1	156	20.2	2	3	2	9.8	10.5	2.4
64	2	1	1	2	176	20.8	1	3	2	9.5	11	2.05
67	2	1	1	2	145	19.4	2	3	2	10.8	16	1.7
55	1	1	1	2	123	21	2	3	2	10.3	19	1.8
75	1	2	1	2	234	22	2	2	1	12.3	18	3.2

56	1	2	1	2	125	20	2	3	2	10.5	15	2.5
66	1	2	2	1	100	23.3	2	3	2	10.6	14	2.3
54	1	2	2	1	167	23	2	3	2	10.5	17	2.2
58	2	2	2	2	176	21	2	3	2	10.3	16	2.1
68	2	1	2	2	123	19.8	2	3	2	9.3	17	1.7
45	2	1	2	2	145	18.4	2	3	2	11.2	12	1.8
49	1	1	1	2	198	19.3	2	3	2	11.9	15	1.33
59	1	2	1	2	187	20.2	2	2	1	11.9	19	2.7
60	1	2	1	2	176	23.9	2	3	2	10.2	18.5	2.3
61	1	2	1	2	156	24	2	3	2	9.8	15	2.8
66	1	2	1	1	144	24.4	2	3	2	9.9	11	2.8
68	1	1	1	1	199	21.1	2	3	2	10.9	12	2.1
46	1	1	1	1	188	22	2	3	2	11.4	15	2.9
75	1	1	1	1	233	20.5	2	2	1	12.1	19	3.3
49	2	1	2	2	266	23	1	2	1	14	17	3.1
56	1	1	1	1	254	28	1	2	1	13.5	20	3.5
57	2	2	2	2	188	20.9	1	2	1	12	21	3.8
67	2	2	1	2	155	23	1	3	2	10.3	14	2.7
64	1	2	2	1	177	21.8	1	3	2	11.9	12	2.6
62	1	2	1	2	233	23	1	2	1	13.12	19	3.1
60	1	2	2	2	111	21.9	2	3	2	9.9	16	2.7
50	2	2	1	2	109	20.3	2	3	2	10.3	14	2.1
67	1	1	1	2	200	21.1	2	3	2	10	10	1.9
45	1	1	1	2	277	20.9	2	2	1	13.2	19.5	3.6
55	1	1	1	1	234	29.4	2	1	1	12.7	20	3.2
44	2	1	1	2	344	27.4	2	2	1	12.12	22	3.21
36	2	1	1	2	211	23.3	2	1	1	13.4	21	3.6
46	1	2	1	1	222	22.2	2	3	2	14.3	17.7	3.6
45	1	2	1	1	122	21.9	2	3	2	12	16	1.9

70	1	2	1	2	134	23	2	3	2	11.4	12	1.88
67	2	2	1	2	156	21.8	2	3	2	11.3	13	2.44
68	1	2	1	2	176	22.7	2	3	2	10.2	13	2.56
65	1	2	2	2	144	21.7	2	3	2	9.5	12	2.5
56	1	2	2	2	155	23.7	2	3	2	9.5	16	2.33
57	2	1	1	2	187	24	2	2	1	12.3	20	3.6
58	2	1	1	2	197	21.9	1	2	1	11.8	22	3.2
59	1	1	1	1	197	27	1	2	1	11.8	21	3.2
46	1	1	1	1	123	23.9	1	3	2	9.9	12	2.2
56	1	2	1	1	145	21.8	2	3	2	9.5	13	2.4
54	2	2	1	2	154	22.8	2	3	2	10.5	11	2.77
53	1	2	1	1	222	23.1	2	2	1	13	19	3.9
65	2	2	1	2	155	22.7	2	3	2	11.3	11	2.99
64	1	2	1	1	211	27	2	3	2	11.2	10	2.11
48	1	1	2	2	200	23.8	2	2	1	11.7	19.5	2.95
56	1	1	2	1	166	24.9	2	3	2	10.9	11	2.1
67	1	1	2	2	156	18.4	2	3	2	9.9	10	1.9
68	1	1	2	1	198	19.4	1	3	2	9.9	15	2.37
66	2	1	1	2	178	20.5	1	3	2	9.8	12	2.75
45	2	2	1	2	109	21	1	3	2	11.4	13	1.23
55	2	1	1	2	177	24	1	3	2	11.4	11	1.4
44	1	2	1	1	234	23.6	2	1	1	11.8	19	2.79
65	1	2	1	1	298	25.5	2	1	1	11.4	20	2.7
58	2	2	1	2	222	30.4	2	2	1	11.9	22	3.45
67	2	1	1	2	322	27.7	2	2	1	12.5	22	3.7
45	2	1	1	2	377	24.9	2	2	1	12.2	20.5	3.55
56	1	1	1	2	344	23	2	2	1	12.6	22	3.2
48	1	2	1	2	222	24.4	2	3	2	10.8	14	2.05
59	1	1	2	2	111	22.2	2	3	2	10.8	12	2.23

39	2	2	2	2	211	23.3	2	3	2	11.1	9	2.9
56	2	1	2	2	266	21.9	2	2	1	12.8	18	2.5
67	2	2	2	2	333	24.4	2	1	1	13	19	2.99
68	2	1	2	2	156	26.6	1	3	2	11.3	11	3.5
53	2	2	2	2	166	20.8	1	1	1	12.6	19	2.87
54	2	1	1	2	155	22.4	1	3	2	9.5	14	2.13
64	1	2	1	1	132	21	1	3	2	9.6	14	2.1
60	1	2	1	1	176	18.5	2	3	2	9.6	16	2.9
62	1	2	1	1	198	19.5	2	3	2	9.6	13	1.76
56	1	1	1	1	176	17.5	2	3	2	9.5	9	1.95
59	1	1	1	2	187	20.1	2	3	2	11.3	10	2.55
66	1	2	1	2	155	22.4	1	3	2	10.3	13	1.1
45	1	2	1	2	154	23.8	1	3	2	9.5	16	1.55
56	1	1	1	2	344	21.1	1	1	1	11.5	22	3.12
67	2	2	1	2	238	25.5	1	2	1	13.5	21	3.2
75	2	2	1	2	200	25	1	2	1	13.2	20.8	3.56
47	2	1	1	2	276	28	2	2	1	12.5	21	3.44
68	1	2	1	1	265	26.6	2	2	1	13.5	21	3.11
67	1	1	1	1	230	21.8	2	1	1	12.8	23	2.99
39	1	2	1	1	300	25.5	2	1	1	12	20	3.22
49	1	1	1	1	231	22.9	2	2	1	11.8	19	3.65
59	1	1	2	1	199	22.9	2	3	2	11.5	10	2.4
66	1	1	2	2	176	21.1	2	3	2	10.9	11	2.85
55	2	1	2	2	300	26.9	2	1	1	12.7	22	2.77
56	2	2	1	2	222	20.5	2	1	1	13.7	20	2.6